Enantioselective radical-chain hydrosilylation of alkenes using homochiral thiols as polarity-reversal catalysts

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The thiol-catalysed radical-chain additions of triphenylsilane and of tris(trimethylsilyl)silane to a number of cyclic prochiral terminal alkenes have been carried out at 60 °C in the presence of di-*tert*-butyl hyponitrite as initiator. The function of the thiol catalyst is to promote the overall abstraction of hydrogen from the silane by the nucleophilic carbon-centred radical intermediate, formed by addition of the silyl radical to the alkene, and the stereogenic centre in the final adduct is set by hydrogen-atom transfer from the thiol to this β-silylalkyl radical. When the thiol is homochiral the transfer of hydrogen becomes enantioselective and an optically active adduct results. A number of homochiral thiols were investigated and the highest enantiomeric excesses (up to 95%) were achieved using the tetra-*O*-acetyl derivatives of 1-thio-β-D-glucopyranose and 1-thio-β-D-mannopyranose. The absolute configuration of an enantiopure triphenylsilane adduct (upgraded by recrystallisation) was determined by X-ray crystallography and it was shown that this adduct could be oxidatively desilylated to the corresponding alcohol and acetate with no loss of enantiomeric purity.

Free-radical reactions are now well established within the repertoire of synthetic methods available to the organic chemist[1] and, in recent years, efforts to control the stereochemistry of these reactions have been at the forefront of research in this area.[2] However, enantioselective atom-transfer processes[3] have received little attention and do not feature in a recent monograph devoted to the stereochemistry of radical reactions.[2]

Enantioselective atom transfer from and to carbon, mediated by a homochiral radical $\overset{*}{X}{}^{\bullet}$ and the closed shell molecule $\overset{*}{X}Y$, is generalised in equation (1). This reaction proceeds through

$$\overset{*}{X}{}^{\bullet} + YCabc \rightleftharpoons \overset{*}{X}Y + {}^{\bullet}Cabc \qquad (1)$$

1a **1b**

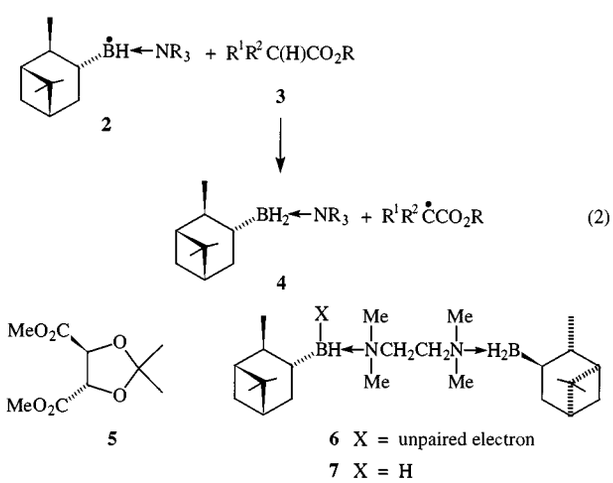
the diastereoisomeric pair of transition states **1a** and **1b** and it is the energy difference between these two structures that determines the enantioselectivity of the transfer of the atom (or group) Y.

For some time, we have been interested in enantioselective hydrogen-atom transfer in connection with our applications of the concept of polarity-reversal catalysis[4,5] of radical reactions. For example, we have shown that homochiral amine-boryl radicals of the type **2** abstract hydrogen enantioselectivity from the electron-deficient α-C–H group of a chiral ester **3**.[3d,6] Although the observed enantioselectivities were generally not large, for some systems investigated the selectivity was sufficient to enable effective *catalytic* kinetic resolution of **3**, during which the amine-boryl radical **2** is regenerated from the amine-borane **4** by hydrogen-atom transfer to the *tert*-butoxyl radical. Thus, the (*S*,*S*)-enantiomer **5** of dimethyl 2,3-*O*-isopropylidenetartrate is 21-times more reactive than the (*R*,*R*)-enantiomer towards the amine-boryl radical **6** at −85 °C.[6a]

† Correspondence concerning the X-ray crystallography should be directed to this Author.

When di-*tert*-butyl peroxide was photolysed in the presence of the racemic tartrate and a catalytic amount of the amine-borane **7**, the tartrate that remained after 75% had been consumed showed a 97% enantiomeric excess (ee) in favour of the (*R*,*R*)-ester.[6b]

The diastereoisomeric transition states **1a** and **b** can be approached from the other direction, *i.e.* by attack of the homochiral reagent $\overset{*}{X}Y$ at the *Re* or *Si* face of the prochiral radical abcC$^{\bullet}$. We have shown that thiols act as polarity-

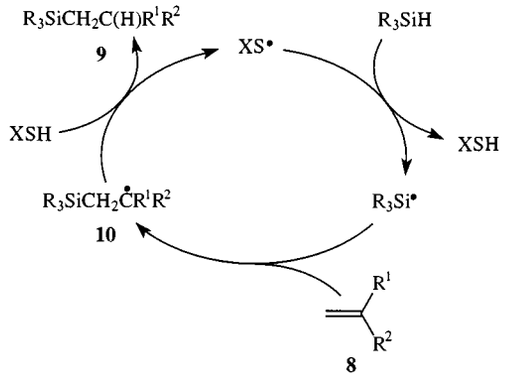


2 **3** **4** **5** **6** X = unpaired electron **7** X = H

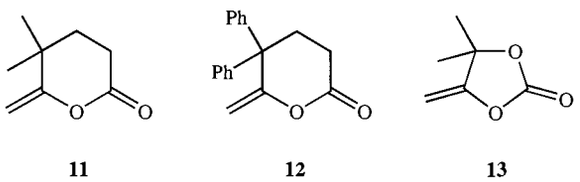
reversal catalysts to promote the radical-chain addition of silanes to alkenes,[7] through the propagation sequence illustrated in Scheme 1. For hydrosilylation of a prochiral alkene **8**, the stereogenic centre in the product silane **9** is formed by hydrogen-atom transfer from the thiol to the prostereogenic radical centre in structure **10**. In a preliminary communication,[8] we have reported that homochiral thiol catalysts can be used to mediate enantioselective hydrosilylation of prochiral alkenes and, in the present paper, we give a fuller account of this work.

Results and discussion

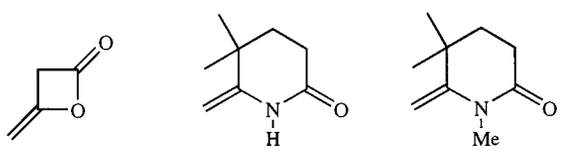
In the light of our preliminary results,[8] the prochiral alkenes **11**–**16** and the homochiral carbohydrate-derived thiols **17**–**24**



Scheme 1



11 **12** **13**



14 **15** **16**

were chosen for further investigations of enantioselective hydrosilylation. Our early work on thiol-catalysed radical-chain hydrosilylation of alkenes[7] was carried out using mainly triethylsilane and *tert*-dodecanethiol‡ (TDT). Under these conditions, adduct yields were substantially improved by adding the thiol catalyst slowly, using a syringe pump, to the reaction mixture containing alkene, silane and initiator. In these experiments, loss of the thiol catalyst occurs as a result of its overall addition to the alkene because, although addition of the thiyl radical to the alkene is reversible, the β-thioalkyl radical so formed is trapped irreversibly by the thiol. Subsequent work showed that methyl thioglycolate (MeO_2CCH_2SH) and, especially, triphenylsilanethiol (TPST) are generally more effective hydrosilylation catalysts than TDT and, with arylsilanes (especially with triphenylsilane) it is often not necessary to add the thiol slowly and all the reagents can be present in the initial reaction mixture. This is partly a consequence of the relative weakness of the Si–H bond in triphenylsilane, as compared with that in a trialkylsilane.[9–11] It is also likely to reflect the greater strength of the S–H bond in TPST,[5c,g] as compared with that in an alkenethiol, and the greater electrophilicity of $Ph_3SiS^{\bullet}$, as compared with that of an alkanethiyl radical, properties which both favour abstraction of hydrogen from the silane by the silanethiyl radical. The corresponding rate-enhancing effects for silanethiyl-radical addition to the alkene are evidently smaller.

Homochiral thiols

The β-glucopyranose derivatives **17** and **21** are available commercially. The β-galactopyranose **18**[12] was prepared from the corresponding α-pyranosyl bromide and the epimeric furanose derivatives **23**[13] and **24**[13] were prepared by reduction of the corresponding thiocyanates, themselves prepared by S_N2 reactions of the epimeric triflates[14] with potassium thiocyanate. The tetra-*O*-trimethylacetyl (pivaloyl) analogue **22** of the acetate **17** was prepared by treatment of the corresponding α-pyranosyl bromide with thiourea, followed by hydrolysis of the thiopseudouronium salt with aq. sodium metabisulfite, according to the standard procedure used to prepare the thiols **17** and **18**. The α- and β-mannopyranose derivatives **19** and **20** were prepared in a similar way. Thus, treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide with thiourea gave mainly the *S*-α-mannosylthiopseudouronium salt[15] by an S_N1 mechanism involving attack of the sulfur nucleophile on the α-face of the intermediate 1,2-acetate-bridged cation.[16] Hydrolysis of this salt gave the α-thiol **19**, which has been described previously.[15] However, a small amount of the β-thiol **20** was also obtained and this compound crystallised particularly well from ethanol, thus facilitating its isolation. The identity of the β-thiol was confirmed by X-ray crystallography and the structure is shown in Fig. 1.

‡ This is the isomeric mixture of thiols *tert*-$C_{12}H_{25}SH$, as obtained from the Aldrich Chemical Co.

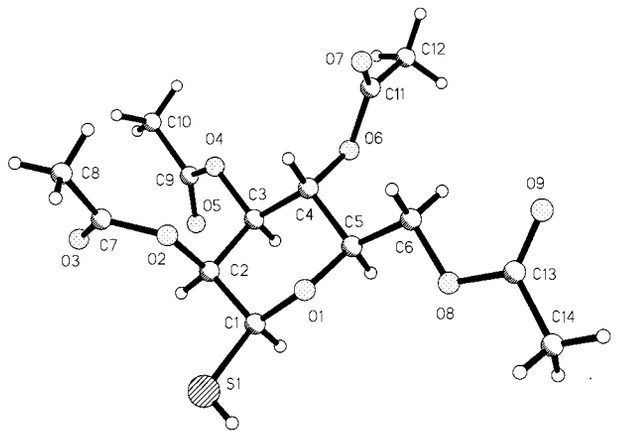
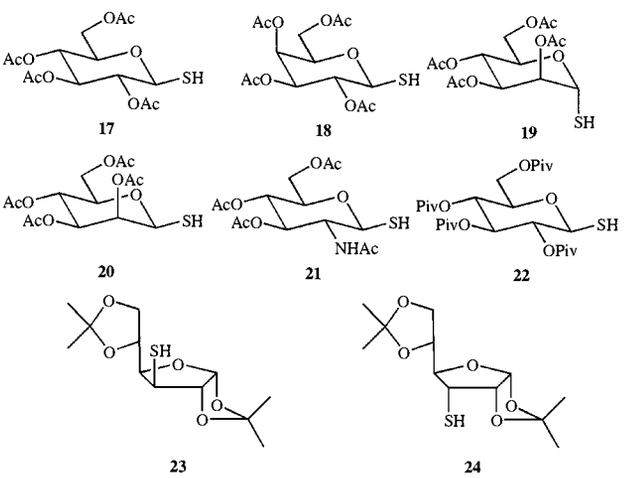


Fig. 1 Structure of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-mannopyranose **20** determined by X-ray crystallography. Selected geometrical parameters (bond lengths in Å, bond angles in degrees): C1–S1 1.829(6), C1–O1 1.453(6), C1–C2 1.529(8), C2–C3 1.564(7), C3–C4 1.534(7), C4–C5 1.556(6), C5–O1 1.464(6), C5–C6 1.512(8); S1–C1–C2 111.8(4), S1–C1–O1 108.1(4), O1–C1–C2 110.7(4).



17 **18** **19**

20 **21** **22**

23 **24**

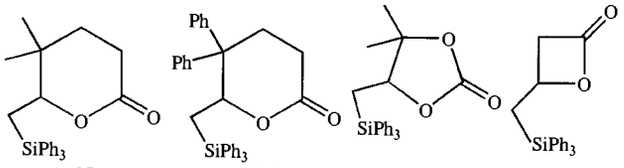
Hydrosilylation using achiral thiol catalysts

Racemic triphenylsilane adducts **25**–**30** were prepared from the alkenes **11**–**16** by radical-chain hydrosilylation initiated by di-*tert*-butyl hyponitrite[17] (TBHN) at 60 °C [equation (3)];§ the

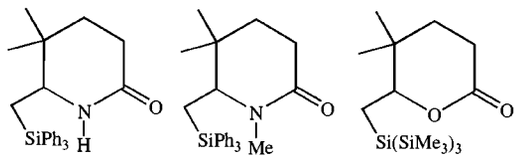
$$Bu^tON{=}NOBu^t \longrightarrow 2Bu^tO^{\bullet} + N_2 \qquad (3)$$

tris(trimethylsilyl)silane[18] adduct **31** was prepared similarly by addition to alkene **11**. The *tert*-butoxyl radicals will go on to abstract hydrogen from the silane and/or the thiol to begin the chain-propagation cycle shown in Scheme 1. Typically, a solution in dry hexane (4 cm^3) containing the methylenelactone **11**

§ The half-life of TBHN at 60 °C is *ca.* 55 min.[17a]



25 **26** **27** **28**



29 **30** **31**

(2.50 mmol), triphenylsilane (3.25 mmol), TBHN (0.125 mmol) and TDT (0.125 mmol) was stirred and heated under argon at 60 °C for 2.5 h. After removal of the solvent by evaporation, the residue was purified by flash chromatography on silica gel to afford the adduct **25** in 54% yield. Examination of the crude product by ^{1}H NMR spectroscopy before purification indicated a yield of 64% and, in the absence of thiol under otherwise identical conditions, the crude yield was ⩽1%. When the TDT was replaced by TPST (5 mol% based on alkene), the isolated yield of **25** rose to 82% (crude yield >90%); yields were similar in hexane or 1,4-dioxane or in mixtures of these two solvents. In succeeding experiments the catalyst is TPST unless stated otherwise.

The isolated yield of the lactone **26** was relatively poor (40% in hexane–1,4-dioxane, 5 : 1), but was very much improved when the pyranose thiols **17** and **20** were used as catalysts (see later). The low yield obtained with TPST may be a result of steric hindrance to hydrogen-atom transfer between this bulky thiol and the bulky adduct radical. The isolated yields of products **27** (hexane solvent), **29** (hexane–1,4-dioxane, 1 : 1) and **30** (hexane) were 50, 65 and 52%, respectively. Although the crude yield of the β-lactone **28** was ~90%, this compound tended to decompose on silica gel and was best isolated by recrystallisation from benzene–hexane. The tris(trimethylsilyl)silane adduct **31** was also obtained in good yield (78% in hexane solvent) using TPST as catalyst, but a 44% yield was obtained in the absence of thiol catalyst under otherwise identical conditions, a consequence of the fact that this silane is a better hydrogen-atom donor than is Ph_3SiH.[18]

The rate constant for abstraction of hydrogen from triphenylsilane by a primary alkyl radical can be estimated to be ~1×10^4 dm^3 mol^{-1} s^{-1} at 60 °C, using data in the literature.[9,10] The rate constant for abstraction of hydrogen from 2-methylpropane-2-thiol (Bu^{t}SH) by a primary alkyl radical is ~10^3 times larger at the same temperature.[19] The more nucleophilic tertiary oxygen- or nitrogen-conjugated β-silylalkyl radicals, formed by addition of silyl radicals to the alkenes **11**–**16**, are likely to show an even greater preference to abstract the electron-deficient hydrogen from the thiol rather than the electron-rich hydrogen from the silane. Alkyl radicals abstract hydrogen from tris(trimethylsilyl)silane more rapidly than from triphenylsilane; at 60 °C the rate constants for abstraction from the former are ~8.8×10^5 and 4.7×10^5 dm^3 mol^{-1} s^{-1} for primary and tertiary radicals, respectively.[20] The corresponding rate constants for abstraction of hydrogen from TDT (*cf.* Bu^{t}SH) should still be appreciably larger but, when only a catalytic amount of thiol is present, abstraction could take place competitively from both hydrogen donors. For thiol-catalysed hydrosilylation with tris(trimethylsilyl)silane, the nature of the substituents on sulfur and at the adduct radical centre will be critically important in determining which molecule is the dominant hydrogen-atom donor.

If the silane is present in excess, some loss of thiol is likely to occur during hydrosilylation as a consequence of the S_H2 processes (4) and (5) (see later),[21] but such reactions should

$$Ph_3Si^{\bullet} + XSH \longrightarrow Ph_3SiSH + X^{\bullet} \quad (4)$$

$$Ph_3Si^{\bullet} + XSH \longrightarrow Ph_3SiSX + H^{\bullet} \quad (5)$$

not become important until after most of the alkene has been consumed, because silyl-radical addition to the alkenes **11**–**16** is very rapid.¶[11,22]

Hydrosilylation using homochiral thiol catalysts

Hydrosilylation of the methylenelactone **11** with triphenylsilane was carried out in the presence of each of the homochiral thiol catalysts **17**–**24** (generally 5 mol% based on alkene) and the results are summarised in Table 1. Chemical yields were high and the effectiveness of these carbohydrate-derived thiols, compared with TDT, as polarity-reversal catalysts is probably related to the relatively high electrophilicities of the derived thiyl radicals and to the relatively high strengths of the S–H bonds in these compounds, as a result of the presence of several electronegative oxygen atoms in the thiols **17**–**24**. The ee of the product **25** varied greatly depending on the nature of the thiol, and the highest enantiomeric purities were obtained using the β-glucose thiol **17** and, especially, the β-mannose thiol **20** (entries 1–3 and 6–8). With the β-mannose thiol, reducing the amount of catalyst from 5 to 1 mol% resulted in only a small reduction in the ee of the adduct (entries 7 and 8). The highest ees were obtained in hexane solvent, although solubility problems sometimes necessitated the use of 1,4-dioxane as a co-solvent. The β-galactose thiol **18** and the 2-acetamido analogue **21** of the β-glucose thiol **17** gave rise to ees somewhat less than that obtained with **17** itself under the same conditions (entries 2, 4 and 9). Somewhat surprisingly, the pivalate analogue **22** of the β-glucose thiol **17** gave rise to an ee slightly smaller than that obtained with the acetate **17**, despite the more bulky acyl groups in the former (entries 2 and 10). The α-mannose thiol **19** afforded adduct which was almost racemic, in sharp contrast to the β-anomer **20** which gave the highest ee (76%) obtained for compound **25** (entries 5 and 6). The SH and 2-acetoxy groups in compound **19** are *trans*, while in the β-anomer **20** they are *cis*, and the very different enantioselectivities obtained can be understood in terms of the asymmetry of the environment around the SH group (see Fig. 1), as presented to the incoming prochiral radical. Molecular models suggest that similar reasons may account for the low ees obtained with the two furanose thiols **23** and **24**, despite the superficial appearance of these molecules when drawn conventionally on paper.

Addition of tris(trimethylsilyl)silane to the methylenelactone **11** was carried out with the thiols **17** and **20** as catalysts in hexane solvent (entries 13 and 14). Again the β-mannose thiol **20** gave the higher ee. Increasing the thiol concentration to 10 mol% did not lead to any significant increase in the ee of the product **31**, indicating that essentially only the thiol is acting as hydrogen donor towards the prochiral adduct radical.

The enantiomeric purity of the adduct **25** was very easily upgraded by recrystallisation and a single crystallisation of 50% ee material from hexane–benzene (2 : 1) was sufficient to give enantiopure material (⩾99.5% ee as judged by HPLC). Crystals suitable for X-ray analysis were obtained for this adduct and the absolute configuration at C-6 was shown to be *R* (see Fig. 2).

¶ EPR studies indicate that the additions of $R_3Si^{\bullet}$ (R = Me, Et or Ph) to the alkenes **11**–**16** are fast ($k_{add} \geqslant 10^3$ dm^3 mol^{-1} s^{-1}) at −80 °C.[23] The radical adducts produced are instantaneously chiral, but stereochemically mobile and exist in the form of rapidly interconverting enantiomeric pairs. We refer to these species as 'prochiral' because, of course, it is not until the stereochemistry is fixed by hydrogen-atom transfer to the three-coordinate radical centre that the isolation of enantiomers becomes possible.

Table 1 Hydrosilylation of 5,5-dimethyl-6-methylenetetrahydropyran-2-one **11** at 60 °C in the presence of homochiral thiol catalysts

Entry	Silane	Thiol[a]	Solvent[b]	Product and yield (%)[c]	Product ee (%)[d]	$[\alpha]_D^{21\pm2}$[e]
1	Ph_3SiH	**17**	D	**25** (63)	40	−31.3 (1.36)
2	Ph_3SiH	**17**	H	**25** (72)	50	−38.8 (1.82)
3	Ph_3SiH	**17**	B	**25** (84)	43	
4	Ph_3SiH	**18**	H	**25** (79)	40	
5	Ph_3SiH	**19**	H	**25** (79)	3	
6	Ph_3SiH	**20**	H	**25** (84)	76	−60.0 (1.38)
7	Ph_3SiH	**20**	B	**25** (82)	60	−47.1 (1.43)
8	Ph_3SiH	**20**[f]	B	**25** (80)	54	
9	Ph_3SiH	**21**	H + D (7:1)	**25** (67)	25	
10	Ph_3SiH	**22**	H	**25** (77)	44	
11	Ph_3SiH	**23**	H	**25** (88)	9	
12	Ph_3SiH	**24**	H	**25** (81)	6	
13	$(Me_3Si)_3SiH$	**17**	H	**31** (92)	47[g,h]	−29.7 (1.16)
14	$(Me_3Si)_3SiH$	**20**	H	**31** (91)	55[h]	−35.7 (1.23)

[a] 5 Mol% based on alkene, unless stated otherwise. [b] D = 1,4-dioxane, H = hexane, B = benzene. [c] Isolated yield. [d] Determined by HPLC analysis, unless stated otherwise, using a Chiralcel-OD column. The (*R*)-(−)-enantiomer of compound **25** was eluted first and was present in excess except for entries 5, 11 and 12. [e] $CHCl_3$ solvent; *c* (g/100 cm^3) shown in parentheses. [f] 1 Mol% thiol present. [g] With 10 mol% thiol the ee (48%) was essentially unchanged. [h] Determined by ^1H NMR spectroscopic analysis using $Eu(hfc)_3$.

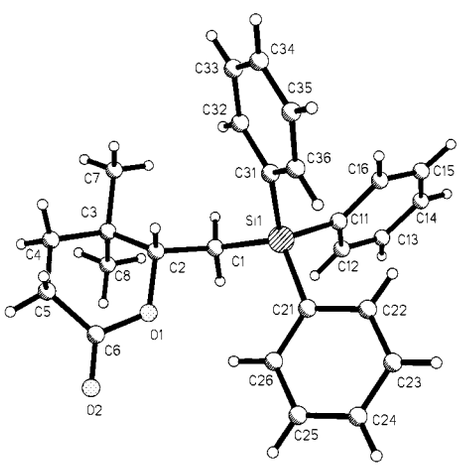
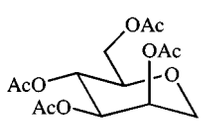


Fig. 2 Structure of (*R*)-(−)-5,5-dimethyl-6-(triphenylsilylmethyl)-tetrahydropyran-2-one (*R*)-**25** determined by X-ray crystallography. Selected geometrical parameters (bond lengths in Å, bond angles in degrees): Si1–C1 1.883(3), Si1–C11 1.865(3), Si1–C21 1.889(3), Si1–C31 1.878(3), C1–C2 1.517(4), C2–C3 1.530(5), C2–O1 1.459(4), O1–C6 1.333(4), C6–O2 1.209(5); C11–Si1–C31 108.3(2), C1–Si1–C11 106.19(14), C1–Si1–C31 108.6(2), C11–Si1–C21 106.0(2), O1–C2–C1 104.2(3), O1–C2–C3 110.2(3), C1–C2–C3 117.0(3).

To demonstrate the viability of the method for organic synthesis, the one-pot enantioselective addition of triphenylsilane to the methylenelactone **11**, catalysed by the β-mannose thiol **20** (5 mol%), was carried out on a 75 mmol scale in hexane solvent. Enantiomerically pure (*R*)-adduct **25** crystallised out of solution during this reaction, but the average ee of the product was 74% and the total yield was 78%, results similar to those obtained on the 2.5 mmol scale (Table 1, entry 6). 2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-mannitol[24] **32** was isolated



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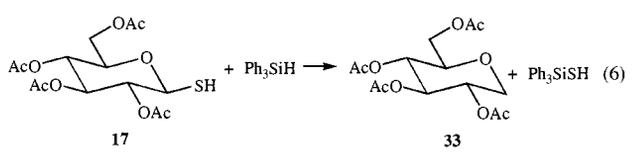
chromatographically from the crude reaction product and is presumably formed by the radical-chain desulfurisation of the thiol catalyst *via* the S_H2 reaction at sulfur shown in equation (4).

The origin of compound **32** was confirmed by treating the β-glucose thiol **17** with triphenylsilane (1.2 equiv.) and TBHN (5 mol% based on thiol) in 1,4-dioxane at 60 °C, when 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-glucitol[25] **33** was isolated in 91% yield [equation (6)]; no reaction occurred in the absence of



17 **33**

TBHN. As was pointed out before, it is likely that desulfurisation of the thiol catalyst takes place to a significant extent only after most of the alkene has been consumed. Desulfurisation of a homochiral thiol catalyst by triphenylsilane produces achiral TPST and, if the latter were to be formed in significant amounts in the early stages of the hydrosilylation, this could result in a product of lower ee than would be obtained if the homochiral thiol were the only hydrogen-atom donor present. When a mixture of the β-glucose thiol **17** (2.5 mol%) and TPST (2.5 mol%) was used as catalyst for the hydrosilylation of the methylenelactone **11**, otherwise under the same conditions as entry 2, the adduct **25** was isolated in 80% yield and showed an ee of 30%. If the two thiols are equally reactive donors of hydrogen to the β-silylalkyl radical adduct, an ee in the region of 25% would be expected, because with thiol **17** alone as catalyst the ee of the adduct was 50%. This result suggests that desulfurisation of the homochiral thiol catalyst causes no major problems in the present work, but the potential effects of this side reaction should always be borne in mind. It is noteworthy that the desulfurization of thiol **17** by triphenylsilane in the absence of alkene proceeds in high yield under mild conditions; the thiol here serves as a polarity-reversal catalyst for its own reduction!

If hydrogen-atom transfer from the homochiral thiol to the prochiral β-silylalkyl radical were to be reversible under the reaction conditions, then partial racemisation of the adduct **25** could take place during the hydrosilylation.[26] To investigate this possibility, enantiopure compound (*R*)-**25** was heated at 60 °C in benzene for 2.5 h in the presence of TBHN (5 mol%) and either TPST (5 mol%) or the β-glucose thiol **17** (5 mol%). In both cases, there was no detectable decrease in the enantiomeric purity of compound **25**, nor was any of the adduct consumed.

The addition reactions of triphenylsilane with the alkenes **12**–**16** were carried out using the pyranose thiols **17**–**22** as catalysts (5 mol%) and the results are summarised in Table 2. The ees of the adduct **26** obtained from the methylenelactone **12** were consistently higher than those achieved with its *gem*-dimethyl analogue **11** (entries 1–8) and, presumably, the extra bulk of the two phenyl groups attached to C-5 in the transition

Table 2 Hydrosilylation of the alkenes **12**–**16** with triphenylsilane at 60 °C in the presence of homochiral thiol catalysts

Entry	Alkene	Thiol[a]	Solvent[b]	Product and yield (%)[c]	Product ee (%)[d]	$[\alpha]_D^{21\pm2}$[e]
1	**12**	**17**	D	**26** (88)	80	−158.7 (1.20)
2	**12**	**17**	B	**26** (92)	86	
3	**12**	**17**	H + D (5:1)	**26** (93)	87	
4	**12**	**18**	H + D (5:1)	**26** (96)	84	
5	**12**	**19**	H + D (5:1)	**26** (92)	5	
6	**12**	**20**	H + D (5:1)	**26** (90)	95	−187.9 (1.21)
7	**12**	**20**	B	**26** (95)	93	
8	**12**	**22**	H + D (5:1)	**26** (95)	87	
9	**13**	**17**	H	**27** (96)	31	−13.1 (1.35)
10	**13**	**20**	H	**27** (76)	55	−24.0 (1.24)
11	**14**	**17**	H + D (5:1)	**28** (40)[f]	5	
12	**15**	**17**	H + D (8:1)	**29** (31)	29	−16.9 (0.66)
13	**15**	**20**	H + D (8:1)	**29** (33)	41	
14	**15**	**21**	H + D (8:1)	**29** (25)	9	
15	**16**	**17**	H	**30** (43)	5	
16	**16**	**20**	H	**30** (48)	5	

[a] 5 Mol% based on alkene. [b] D = 1,4-dioxane, H = hexane, B = benzene. [c] Isolated yield. [d] Determined by HPLC analysis, using a Chiralcel-OD column (entries 1–11, major enantiomer eluted first) or a Chiralpak-AD column (entries 12–16, major enantiomer eluted second). [e] $CHCl_3$ solvent; *c* (g/100 cm^3) shown in parentheses. [f] Crude yield 57%.

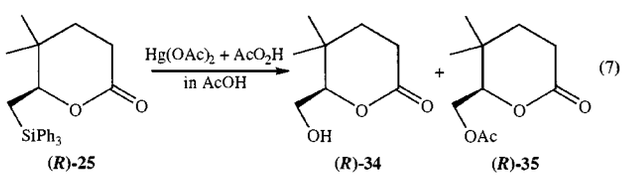
state leading to adduct **12** is responsible for the difference. The highest ee obtained (95%), with the β-mannose thiol **20** in hexane–1,4-dioxane (entry 6), is remarkably large and very encouraging; the chemical yields were consistently high. The ees obtained with the cyclic carbonate **13** (entries 9 and 10) were quite similar to those of the adducts derived from compound **11**, as might be expected in view of the similar structures of the intermediate β-silylalkyl radicals. The ee of the adduct obtained from diketene **14** with the β-glucose thiol as catalyst was very small (5%), again as anticipated because of the very similar sizes of the two endocyclic substituents attached to the radical centre in the intermediate β-silylalkyl radical.

As was found with the isoelectronic methylenelactone **11**, the ee of the adduct **29** derived from the methylenelactam **15** with the β-mannose thiol **20** as catalyst was greater than that obtained with the β-glucose thiol **17** (entries 12 and 13). Only a very modest ee was achieved for adduct **29** with the β-glucosamine derivative **21** as catalyst (entry 14), when hydrogen-bonding interactions between the amide functions in the intermediate β-silylalkyl radical and in the thiol catalyst could possibly be involved in the transition state for hydrogen-atom transfer. The *N*-methyl analogue **16** of the methylenelactam **15** gave the adduct **30** with a very low ee when either pyranose thiol **17** or **20** was used as catalyst.

Desilylation of (*R*)-(−)-5,5-dimethyl-6-(triphenylsilylmethyl)-tetrahydropyran-2-one; (*R*)-25

Oxidative cleavage of an aliphatic carbon–silicon bond in an organosilane[27] can be carried out under either basic[28] or acidic[29] conditions with retention of configuration at the carbon centre. To proceed successfully, an electronegative group must also be attached to silicon and electrophilic aromatic substitution can be used conveniently to convert a *Si*-aryl group into such an activating ligand. At this stage, we have not attempted to find optimal conditions for the oxidative desilylation of our chiral adducts, but we have applied the one-pot methodology introduced by Fleming *et al.*[29] to the cleavage of the adduct (*R*)-(−)-**25** as an illustrative example.

Treatment of compound (*R*)-**25** with a total of 3.2 mol equiv. of mercury(II) acetate in the presence of an excess of commercial peroxyacetic acid in acetic acid over a period of 6 days at room temperature (rt) afforded a mixture of the alcohol (*R*)-**34** and the acetate (*R*)-**35** in a total yield of 63% [equation (7)]. Under these conditions, it was possible to avoid any Peterson-type elimination which would lead to ring opening and loss of chirality. Although the chiral centre in substrate **25** is β to silicon, HPLC analysis was used to confirm that no loss of optical



(7)

purity had occurred during desilylation, by comparison with the racemic compounds obtained from the racemic adduct (±)-**25**. In most of the examples reported by Fleming,[29] this method was used for the cleavage of secondary alkyl–silicon bonds and only the corresponding secondary alcohol was isolated. Commercial peroxyacetic acid solution contains a small amount of sulfuric acid and this, together with the relatively long reaction time and the fact that compound **34** is a primary alcohol, evidently results in considerable esterification of the latter to give the acetate **35**.

Conclusions

The development of enantioselective atom-transfer processes as a tool in asymmetric synthesis is still in its infancy. Some of the reactions reported in this work proceed with good enantioselectivity at moderately high temperatures and the results are very encouraging, particularly in view of the fact that the source of chirality is a potentially recyclable and metal-free thiol catalyst. Furthermore, the optically active adducts formed by hydrosilylation can be oxidatively desilylated to provide a variety of useful silicon-free organic compounds. Taking a negative standpoint, it might be argued that bulky substituents are needed on both the alkene and the silane in order to achieve a high enantiomeric excess in the adduct. This may be so at present, but the potential of the method is clearly proven and future development can focus on the design of new thiol catalysts which are capable of reacting with high enantioselectivity with less sterically encumbered radical intermediates.

Experimental

NMR spectra were recorded using a Varian VXR-400 instrument (400 MHz for ^1H). The solvent was $CDCl_3$ and chemical shifts are reported relative to Me_4Si; *J*-values are quoted in Hz. IR spectra were recorded using a Perkin-Elmer 1600 Series FTIR spectrometer. Column chromatography and TLC were carried out using Merck Kieselgel 60 (230–400 mesh) and Kieselgel 60 F_{254} aluminium-backed pre-coated plates, respectively. Mass spectra were obtained with VG 7070H or

Micromass Quattro LC instruments using electron impact ionisation (EI), atmospheric pressure chemical ionisation (APCI) or chemical ionisation (CI) with ammonia. Determination of ee by high-performance liquid chromatography (HPLC) was carried out using Chiralcel-OD or Chiralpak-AD columns (4.6 mm × 250 mm; Daicel Chemical Industries Ltd.) in conjunction with hexane–isopropyl alcohol eluent (flow rate 1 cm^3 min^{-1}). The proportion of alcohol in the eluent is given in the text and UV detection was at 254 nm (unless stated otherwise). Optical rotations were measured on an AA Series Polaar 2000 polarimeter (Optical Activity Ltd.) using a 1 dm cell and are given in units of 10^{-1} deg cm^2 g^{-1}.

All manipulations and reactions of air-sensitive compounds were carried out under dry argon or nitrogen and all extracts were dried over anhydrous $MgSO_4$. Light petroleum refers to the fraction of distillation range 40–60 °C.

Materials

1,4-Dioxane, benzene and hexane (Aldrich 95+% HPLC grade) were heated under reflux over calcium hydride and distilled and stored under argon. TBHN was prepared by the reaction of sodium hyponitrite with *tert*-butyl bromide in diethyl ether, in the presence of zinc chloride, using the method described by Mendenhall.[17b] Triphenylsilanethiol, *tert*-dodecanethiol, 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose **17** and its 2-acetamido analogue **21** were obtained commercially (Aldrich) and were used as received.

Prochiral alkenes

The methylenelactone **11**[30] and the corresponding lactam **15**[30] were prepared as described below by modifications of procedures in the literature. The alkenes **12**[31] and **13**[32] were prepared as described previously and diketene **14** was obtained commercially (Aldrich) and distilled immediately before use. The preparation of the methylenelactam **16** and data for other alkenes that have not been adequately characterised previously are given below.

5,5-Dimethyl-6-methylenetetrahydropyran-2-one 11. This lactone was prepared as descried[30] by the cyclodehydration of 4,4-dimethyl-5-oxohexanoic acid, except that the dehydrating agent used was isopropenyl acetate (rather than acetyl chloride) and the procedure followed was that described for the preparation of analogue **12**.[31] Bp 42–44 °C/0.1 mmHg (lit.,[30] 95–96 °C/10 mmHg); δ_H 1.20 (6 H, s, CMe_2), 1.68 (2 H, t, *J* 7.2, CH_2CMe_2), 2.64 (2 H, t, *J* 7.2, CH_2CO), 4.34 (1 H, d, *J* 2.0, vinyl H) and 4.62 (1 H, d, *J* 2.0, vinyl H); δ_C 25.9, 27.1, 31.8, 32.6, 91.2, 163.2 and 167.8; *m*/*z* (EI) 140 (M^+, 54%), 112 (36), 96 (53), 70 (59) and 44 (100).

6-Methylene-5,5-diphenyltetrahydropyran-2-one 12. Mp 137–138 °C (lit.,[31] 138.5–139.5 °C); δ_H 2.55 (2 H, t, *J* 6.8, CH_2CPh_2), 2.75 (2 H, t, *J* 6.8, CH_2CO), 3.90 (1 H, d, *J* 1.8, vinyl H), 4.99 (1 H, d, *J* 1.8, vinyl H) and 7.20–7.37 (10 H, m, Ph); δ_C 28.4, 29.9, 51.4, 99.1, 127.4, 128.2, 128.6, 142.1, 160.4 and 167.3.

5,5-Dimethyl-6-methylenepiperidin-2-one 15. Ammonia (~20 cm^3) was slowly condensed onto the methylenelactone **11** (20.0 g, 0.14 mol) and the resulting slurry was then stirred for 15 min before the excess of ammonia was allowed to evaporate off. Toluene (60 cm^3) was added to the residual 4,4-dimethyl-5-oxohexanamide and the mixture was heated under reflux using a Dean-and-Stark apparatus to bring about dehydration. The toluene was removed under reduced pressure and the residual solid was recrystallised from dichloromethane–hexane to give the methylenelactam **15** (15.7 g, 81%), mp 108–109 °C (lit.,[30] 108–109 °C); δ_H 1.15 (6 H, s, CMe_2), 1.59 (2 H, t, *J* 6.8, CH_2CMe_2), 2.44 (2 H, t, *J* 6.8, CH_2CO), 4.12 (1 H, d, *J* 1.1, vinyl H), 4.25 (1 H, d, *J* 1.1, vinyl H) and 8.91 (1 H, br s, NH); δ_C 27.0, 28.6, 32.3, 33.4, 89.5, 150.1 and 171.0; *m*/*z* (APCI) 140 (M^+ + 1, 100%).

1,5,5-Trimethyl-6-methylenepiperidin-2-one 16. This was prepared in the same way as compound **15**, starting from the methylenelactone **11** (15.0 g, 0.11 mol) and methylamine (~15 cm^3), and was obtained as an oil (14.1 g, 84%), bp 50 °C/0.2 mmHg; δ_H 1.13 (6 H, s, CMe_2), 1.58 (2 H, t, *J* 7.0, CH_2CMe_2), 2.50 (2 H, t, *J* 7.0, CH_2CO), 3.10 (3 H, s, NMe) and 4.30 (2 H, s, vinyl H); δ_C 27.7, 29.4, 31.0, 33.2, 33.9, 90.2, 154.2 and 169.2; *m*/*z* (APCI) 154 (M^+ + 1, 100%) and 141 (15) (Found: C, 70.2; H, 9.9; N, 9.2. $C_9H_{15}NO$ requires C, 70.55; H, 9.87; N, 9.14%).

Preparation of homochiral thiols

The β-galactopyranose thiol **18**,[12] the α-mannopyranose thiol **19**[15] and the epimeric furanose derivatives **23**[13,14] and **24**[13,14a,b] were prepared according to methods in the literature; where these compounds have been inadequately characterised previously, further data are given below.

2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-galactopyranose 18.[12] Mp 86–88 °C (lit.,[12b] 86.5–88 °C); $[\alpha]_D^{19}$ +38.0 (*c* 2.62, $CHCl_3$) {lit.,[12b] $[\alpha]_D^{19}$ +32.0 (*c* 3.5, $CHCl_3$)}; δ_H 1.93 (3 H, s, Ac), 2.00 (3 H, s, Ac), 2.04 (3 H, s, Ac), 2.12 (3 H, s, Ac), 2.33 (1 H, d, *J* 10.0, SH), 3.91 (1 H, td, *J* 6.6 and ~1.1, H-5), 4.08 (2 H, d, *J* 6.9, H-6), 4.49 (1 H, t, *J* 9.9, H-1), 4.97 (1 H, dd, *J* 10.1 and 3.2, H-3), 5.13 (1 H, t, *J* 10.0, H-2) and 5.38 (1 H, dd, *J* 3.2 and ~1.1, H-4) (the analysis was confirmed by ^1H–^1H decoupling experiments); δ_C 20.5, 20.7 (2 C), 20.8, 61.4, 67.2, 70.8, 71.5, 74.9, 79.1, 169.8, 170.0, 170.1 and 170.4.

2,3,4,6-Tetra-*O*-acetyl-1-thio-α-D-mannopyranose 19.[15] Oil, $[\alpha]_D^{20}$ +78.6 (*c* 0.77, $CHCl_3$) {lit.,[15a] $[\alpha]_D^{20}$ +84.5 (*c* 1, MeOH)}; δ_H 1.99 (3 H, s, Ac), 2.05 (3 H, s, Ac), 2.09 (3 H, s, Ac), 2.15 (3 H, s, Ac), 2.29 (1 H, d, *J* 6.9, SH), 4.10 (1 H, dd, *J* 12.2 and 2.0, H^A-6), 4.29 (1 H, dd, *J* 12.2 and 5.0, H^B-6), 4.35 (1 H, m, H-5), 5.31 (3 H, m, H-2, -3 and -4) and 5.55 (1 H, d, *J* 6.9, H-1) (the analysis was confirmed by ^1H–^1H decoupling experiments); δ_C 20.6(0), 20.6(4), 20.7, 20.8, 62.1, 66.0, 68.5, 69.6, 71.8, 76.9, 169.6, 169.8, 169.9 and 170.6 (Found: C, 46.4; H, 5.5. $C_{14}H_{20}O_9S$ requires C, 46.15; H, 5.53%).

2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-mannopyranose 20. The α-mannose thiol **19** was prepared from the corresponding α-mannosyl bromide (21.3 g, 52 mmol) and thiourea (5.92 g, 78 mmol), according to the procedure given in the literature.[15] The crude thiol was then taken up in an approximately equal volume of ethanol and the solution was kept in a freezer at −20 °C for 4–5 days, when the β-anomer **20** crystallised, leaving the more abundant α-anomer in the mother liquor. Recrystallization of the β-anomer from ethanol afforded the pure thiol **20** (1.43 g, 7.5%), mp 161–162 °C, $[\alpha]_D^{19}$ −29.7 (*c* 0.78, $CHCl_3$); δ_H 1.96 (3 H, s, Ac), 2.02 (3 H, s, Ac), 2.08 (3 H, s, Ac), 2.22 (3 H, s, Ac), 2.52 (1 H, d, *J* 9.8, SH), 3.69 (1 H, ddd, *J* 10.0, 5.4 and 2.4, H-5), 4.10 (1 H, dd, *J* 12.4 and 2.4, H^A-6), 4.22 (1 H, dd, 12.4 and 5.4, H^B-6), 4.87 (1 H, dd, *J* 9.8 and 1.2, H-1), 5.05 (1 H, dd, *J* 10.1 and 3.5, H-3), 5.20 (1 H, t, *J* 10.1, H-4) and 5.42 (1 H, dd, *J* 3.5 and 1.2, H-2) (the analysis was confirmed by ^1H–^1H decoupling experiments); δ_C 20.6(0), 20.6(2), 20.7, 20.8, 62.6, 65.2, 71.6, 72.0, 76.4, 76.9, 169.6, 170.0, 170.1 and 170.7; *m*/*z* (APCI) 387 (M^+ + Na, 12%), 365 (M^+ + 1, 1) and 169 (100) (Found: C, 46.3; H, 5.5. $C_{14}H_{20}O_9S$ requires C, 46.15; H, 5.53%).

2,3,4,6-Tetra-*O*-pivaloyl-1-thio-β-D-glucopyranose 22. A solution of 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranosyl bromide[33] (33.6 g, 58 mmol) and thiourea (4.4 g, 58 mmol) in dry acetone (25 cm^3) was stirred and heated under reflux for 40 min. The mixture was allowed to cool and the acetone was removed under reduced pressure. Tetrachloromethane (75 cm^3) was added to the crude thiopseudouronium salt, followed by aq. sodium metabisulfite (11.0 g, 58 mmol in 45 cm^3). The resulting two-phase mixture was stirred vigorously and heated under reflux for 1 h, allowed to cool and the layers were separated. The organic layer was washed successively with water (40 cm^3) and saturated brine (40 cm^3) and then dried. After removal of the solvent, the residual solid was recrystallised from ethanol to afford the thiol **22** (16.1 g, 54%), mp 115–116 °C; $[\alpha]_D^{20}$ +18.8 (*c* 1.18, $CHCl_3$); δ_H 1.09 (9 H, s, CMe_3), 1.12 (9 H, s, CMe_3),

1.16 (9 H, s, CMe_3), 1.21 (9 H, s, CMe_3), 2.23 (1 H, d, *J* 10.0, SH), 3.72 (1 H, ddd, *J* 10.1, 4.9 and 1.9, H-5), 4.08 (1 H, dd, *J* 12.5 and 4.9, H^A-6), 4.17 (1 H, dd, *J* 12.5 and 1.9, H^B-6), 4.52 (1 H, apparent t, *J* ~9.7, H-1), 4.98 (1 H, t, *J* 9.4, H-2), 5.15 (1 H, apparent t, *J* 9.8, H-4) and 5.27 (1 H, t, *J* 9.4, H-3) (the analysis was confirmed by ^1H–^1H decoupling experiments); δ_C 27.0(1), 27.0(7), 27.1(0), 27.1(3), 38.7(0), 38.7(3) (2 C), 38.9, 61.8, 67.5, 73.0, 73.5, 76.8, 79.0, 176.3, 176.8, 177.1 and 178.0; *m*/*z* (APCI) 555 (M^+ + Na, 10%), 533 (M^+ + 1, 1), 499 (79) and 211 (100) (Found: C, 58.3; H, 8.3. $C_{26}H_{44}O_9S$ requires C, 58.62; H, 8.33%).

Representative procedure for thiol-catalysed hydrosilylation

The methylenelactone **12** (0.660 g, 2.50 mmol), triphenylsilane (0.845 g, 3.25 mmol) and the β-mannose thiol **20** (45.5 mg, 0.125 mmol) were weighed into a 25 cm^3 flat-bottomed flask equipped with a stoppered side-arm, and a stirrer bar was added. The flask was fitted with a short condenser and the apparatus was flushed with argon with the side-arm stopper removed. Hexane (5.0 cm^3) and 1,4-dioxane (1.0 cm^3) were added, followed by TBHN (22 mg, 0.126 mmol) after the reagents had dissolved. The mixture was stirred and heated for 2.5 h at 60 °C, then the solvent was removed by evaporation under reduced pressure and the residue was purified by flash chromatography [eluent: light petroleum–diethyl ether (10:1) (~100 cm^3), followed by light petroleum–diethyl ether (6:1) (~100 cm^3), followed by light petroleum–diethyl ether (3:1) (~200 cm^3)] to afford the adduct **26** as a solid (1.18 g, 90%; 95% ee). When the above reaction was repeated using benzene (6 cm^3) alone as solvent, the results were similar (isolated yield 1.24 g, 95%; 93% ee). In general, the volume of solvent varied between 4 and 6 cm^3 depending on the solubilities of the reagents and the catalyst. In all reactions, care was exercised to take a homogeneous sample of the total product for the determination of ee and optical rotation. The characteristics of the (racemic) adducts are given below.

5,5-Dimethyl-6-(triphenylsilylmethyl)tetrahydropyran-2-one 25. Mp 115–116 °C; δ_H 0.92 (3 H, s, CMe^A), 1.00 (3 H, s, CMe^B), 1.58 (3 H, m, CH_2CMe_2 and $SiCH^A$), 1.79 (1 H, dd, *J* 15.0 and 11.5, $SiCH^B$), 2.40 (2 H, m, CH_2CO), 4.11 (1 H, dd, *J* 11.5 and 2.4, CHO), 7.38 (9 H, m, ArH) and 7.59 (6 H, m, ArH); δ_C 15.0, 19.3, 26.6, 27.4, 33.1, 34.0, 84.6, 127.8, 129.5, 134.5, 135.9 and 170.9; *m*/*z* (EI) 400 (M^+, 1%), 323 (96), 259 (100) and 199 (96) (Found: C, 77.9; H, 7.1. $C_{26}H_{28}O_2Si$ requires C, 77.96; H, 7.05%). The ee was determined using the Chiralcel-OD column [eluent: 1% isopropyl alcohol; t_R 14 (*R*) and 16 (*S*) min].

5,5-Diphenyl-6-(triphenylsilylmethyl)tetrahydropyran-2-one 26. Mp 161–162 °C; δ_H 1.28 (1 H, dd, *J* 15.1 and 1.8, $SiCH^A$), 1.78 (1 H, dd, *J* 15.1 and 11.5, $SiCH^B$), 2.09 (1 H, m, CH^ACPh_2), 2.50 (2 H, m, CH^ACO and CH^BCPh_2), 2.92 (1 H, m, CH^BCO), 5.41 (1 H, br d, *J* ~11.5, CHO) and 7.02–7.47 (25 H, m, Ph); δ_C 17.9, 26.5, 27.5, 49.1, 81.8, 126.6, 126.8, 127.3, 127.6, 127.9, 128.7, 129.6, 134.0, 135.8, 143.8, 144.4 and 169.0 (overlap of two aryl C); *m*/*z* (EI) 524 (M^+, 1%), 259 (65), 222 (100) and 180 (97) (Found: C, 82.1; H, 6.0. $C_{36}H_{32}O_2Si$ requires C, 82.40; H, 6.15%). The ee was determined using the Chiralcel-OD column (eluent: 10% isopropyl alcohol t_R 8 and 11 min).

4,4-Dimethyl-5-triphenylsilylmethyl-1,3-dioxolan-2-one 27. Mp 150–151 °C; δ_H 1.32 (3 H, s, CMe^A), 1.39 (3 H, s, CMe^B), 1.49 (1 H, dd, *J* 15.0 and 3.0, $SiCH^A$), 1.90 (1 H, dd, *J* 15.0 and 11.4, $SiCH^B$), 4.40 (1 H, dd, *J* 11.4 and 3.0, CHO), 7.33–7.55 (15 H, m, Ph); δ_C 14.3, 21.4, 25.2, 83.2, 84.9, 128.1, 130.0, 133.2, 135.7 and 153.7; *m*/*z* (EI) 388 (M^+, 4%), 259 (100), 243 (50) and 199 (95) (Found: C, 74.1; H, 6.15. $C_{24}H_{24}O_3Si$ requires C, 74.19; H, 6.23%). The ee was determined using the Chiralcel-OD column (eluent: 10% isopropyl alcohol; t_R 7 and 8 min).

4-(Triphenylsilylmethyl)oxetan-2-one 28. Mp 91–92 °C; δ_H 1.86 (1 H, dd, *J* 14.1 and 10.8, $SiCH^A$), 2.36 (1 H, dd, *J* 14.1 and 4.4, $SiCH^B$), 2.65 (1 H, dd, *J* 16.5 and 4.4, H^A-3), 3.10 (1 H, dd, *J* 16.5 and 5.7, H^B-3), 4.77 (1 H, m, CHO) and 7.33–7.53 (15 H, m, Ph); δ_C 21.2, 44.5, 70.4, 128.3, 130.2, 132.9, 135.4 and 168.2; *m*/*z* (APCI) 367 (M^+ + Na, 10%), 344 (M^+, 1), 291 (42) and 153 (100) (Found: C, 77.0; H, 5.7. $C_{22}H_{20}O_2Si$ requires C, 76.71; H, 5.85%). The ee was determined using the Chiralcel-OD column (eluent: 20% isopropyl alcohol; t_R 10 and 13 min).

5,5-Dimethyl-6-(triphenylsilylmethyl)piperidin-2-one 29. Mp 129–130 °C; δ_H 0.97 (3 H, s, CMe^A), 0.98 (3 H, s, CMe^B), 1.34 (1 H, dd, *J* 15.0 and 11.7, $SiCH^A$), 1.57 (2 H, m, CH_2CMe_2), 1.75 (1 H, dd, *J* 15.0 and 1.1, $SiCH^B$), 2.27 (2 H, m, CH_2CO), 3.40 (1 H, apparent d, *J* 11.5, CHN), 5.17 (1 H, br s, NH) and 7.37–7.60 (15 H, m, Ph); δ_C 15.3, 18.6, 27.1, 28.4, 33.2, 34.8, 58.2, 128.4, 130.2, 133.5, 135.6 and 171.2; *m*/*z* (EI) 399 (M^+, 20%), 343 (20), 259 (100) and 140 (63) (Found: C, 77.9; H, 7.4; N, 3.35. $C_{26}H_{29}NOSi$ requires C, 78.15; H, 7.31; N, 3.51%). The ee was determined using the Chiralpak-AD column (eluent: 10% isopropyl alcohol; t_R 7 and 11 min).

1,5,5-Trimethyl-6-(triphenylsilylmethyl)piperidin-2-one 30. Mp 131–132 °C; δ_H 0.81 (3 H, s, CMe^A), 0.89 (3 H, s, CMe^B), 1.41 (1 H, dddd, *J* 13.8, 7.9, 3.5 and 1.6, CH^ACMe_2), 1.58 (1 H, dd, *J* 15.5 and 8.2, $SiCH^A$), 1.89 (1 H, dd, *J* 15.5 and 3.7, $SiCH^B$), 2.02 (1 H, dt, *J* 13.8 and 9.0, CH^BCMe_2), 2.36 (2 H, m, CH_2CO), 2.43 (3 H, s, NMe), 3.01 (1 H, ddd, *J* 8.2, 3.7 and 1.6, CHN) and 7.29–7.55 (15 H, m, Ph); δ_C 16.5, 25.7, 27.5, 28.3, 29.2, 34.8, 36.4, 65.8, 128.1, 129.7, 134.3, 135.5 and 169.8; *m*/*z* (EI) 413 (M^+, 20%), 259 (85), 154 (100) and 140 (55) (Found: C, 78.1; H, 7.5; N, 3.55. $C_{27}H_{31}NOSi$ requires C, 78.40; H, 7.55; N, 3.39%). The ee was determined using the Chiralpak-AD column (eluent 5% isopropyl alcohol; t_R 7 and 9 min).

5,5-Dimethyl-6-[tris(trimethylsilyl)silylmethyl]tetrahydropyran-2-one 31. Oil; δ_H 0.18 [27 H, s, $Si(SiMe_3)_3$], 0.91 (3 H, s, CMe^A), 0.96 (3 H, s, CMe^B), 0.99 (1 H, dd, *J* 14.5 and 11.5, $SiCH^A$), 1.06 (1 H, dd, *J* 14.5 and 2.5, $SiCH^B$), 1.63 (2 H, m, CH_2CMe_2), 2.50 (2 H, m, CH_2CO) and 4.01 (1 H, dd, *J* 11.5 and 2.5, CHO); δ_C 1.1, 8.8, 18.6, 26.9, 27.7, 33.6, 34.5, 87.4 and 171.3; *m*/*z* (CI) 406 ($M^+ + NH_4$) and 389 (M^+ + H) [Found: (CI) (M^+ + 1), 389.2207. $C_{17}H_{40}O_2Si_4$ requires (*M* + 1), 389.2184]. The ee was determined by ^1H NMR analysis using (+)-tris[3-(heptafluoropropylhydroxymethylene)camphorato]europium(III) [Eu(hfc)$_3$] as shift reagent.

Large-scale enantioselective hydrosilylation of compound 11

A solution of the lactone **11** (10.51 g, 75.0 mmol), triphenylsilane (25.35 g, 97.3 mmol), TBHN (0.65 g, 3.75 mmol) and the β-mannose thiol **20** (1.37 g, 3.76 mmol) in hexane (120 cm^3) was stirred and heated at 60 °C for 2.5 h under nitrogen. During the reaction, the enantiomerically pure adduct **25** crystallised out of solution. The reaction mixture was diluted with CH_2Cl_2 to obtain a homogeneous solution and a small aliquot was taken to determine the ee (74%). The solvent was removed by evaporation under reduced pressure and the residual solid was stirred with hexane (100 cm^3) under reflux. The cooled slurry was filtered and the solid was washed on the sinter with cold hexane (2 × 120 cm^3) to give, after drying, (*R*)-(−)-**25** (19.10 g, 64%; >99.5% ee). The filtrate was evaporated under reduced pressure and the residue was purified by flash chromatography [eluent: light petroleum–diethyl ether (10:1), followed by light petroleum–diethyl ether (6:1), followed by light petroleum–diethyl ether (3:1)] to afford the remaining product as a solid [4.15 g, 14%; 17.5% ee in favour of (*S*)-(+)-**25**]. For the enantiopure adduct (*R*)-(−)-**25**, $[\alpha]_D^{22}$ −77.5 (*c* 1.78, $CHCl_3$), mp 135–136 °C.

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-mannitol 32. This compound was isolated by flash chromatography during the purification of the product from the large-scale hydrosilylation using the β-mannose thiol **20** as catalyst. Mp 154–156 °C (lit.,[24c] 154–155 °C); δ_H 2.00 (3 H, s, Ac), 2.04 (3 H, s, Ac), 2.10 (3 H, s, Ac), 2.16 (3 H, s, Ac), 3.59 (1 H, ddd, *J* 9.9, 5.4 and 2.3, H-5),

3.67 (1 H, dd, *J* 13.2 and 1.1, H^A-1), 4.06 (1 H, dd, *J* 13.2 and 2.1, H^B-1), 4.13 (1 H, dd, *J* 12.4 and 2.3, H^A-6), 4.24 (1 H, dd, *J* 12.4 and 5.4, H^B-6), 5.05 (1 H, dd, *J* 10.0 and 3.6, H-3), 5.26 (1 H, t, *J* 10.0, H-4) and 5.31 (1 H, br m, H-2) (the analysis was confirmed by ^1H–^1H decoupling experiments); δ_C 20.6, 20.7, 20.8, 21.0, 62.7, 66.1, 68.1, 68.6, 71.6, 76.7, 169.6, 170.1, 170.3 and 170.7. These NMR data are in agreement with data in the literature.[24c]

Desulfurisation of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose 17. A solution of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucose **17** (364 mg, 1.0 mmol), triphenylsilane (313 mg, 1.2 mmol) and TBHN (8.70 mg, 0.05 mmol) in dry 1,4-dioxane (2.0 cm^3) was stirred at 60 °C for 2.5 h under nitrogen and then allowed to cool to rt. The solvent was removed by evaporation under reduced pressure and the residue was purified by flash chromatography [eluent: light petroleum–diethyl ether (6:1)] to afford 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-glucitol **33** as a solid (304 mg, 91%), mp 73–75 °C (lit.,[25] 73–75 °C). In the absence of initiator, no reaction takes place; δ_H 2.00 (9 H, br s, 3 × Ac), 2.06 (3 H, s, Ac), 3.27 (1 H, t, *J* 10.5, H-4), 3.56 (1 H, ddd, *J* 10.5, 4.9 and 2.3, H-5), 4.07–4.19 (3 H, m, H^A-1 and H-6), 4.94–5.02 (2 H, m, H-2 and -3) and 5.17 (1 H, t, *J* 9.5, H^B-1); δ_C 20.6, 20.7(0) (2 C), 20.7(2), 62.2, 66.8, 68.4, 68.9, 73.7, 76.4, 169.5, 169.7, 170.3 and 170.6.

Desilylation of (*R*)-(−)-5,5-dimethyl-6-(triphenylsilylmethyl)-tetrahydropyran-2-one (*R*)-25

A flask containing the enantiopure (*R*)-adduct **25** (0.50 g, 1.25 mmol), mercury(II) acetate (0.42 g, 1.31 mmol) and a stirrer bar was cooled in an ice-bath and peracetic acid (40% in AcOH; 10.0 cm^3, ~55 mmol) was added with stirring of the mixture. The heterogeneous mixture was warmed to rt and stirred for 2 days, when another equal portion of mercury(II) acetate (0.42 g, 1.31 mmol) was added and stirring was continued for a further 2 days. A third equal portion of mercury(II) acetate was then added and the heterogeneous mixture was stirred for a further 2 days. The mixture was filtered and the solid material was washed on the sinter with dichloromethane (3 × 20 cm^3). The filtrate was co-evaporated with toluene (3 × 50 cm^3) under reduced pressure at 25 °C (to remove the excess of acetic and peroxyacetic acids - *CARE!*) and the residue was purified by flash chromatography [eluent: light petroleum–diethyl ether (10:1), followed by light petroleum–diethyl ether (1:1)] to afford the acetate **35** as an oil (92 mg, 37%). The crude alcohol **34** was obtained by stripping the column with methanol and, after evaporation of the solvent, the residue was purified by flash chromatography [eluent: light petroleum–ethyl acetate (2:1)] to afford the alcohol **34** as a solid (51 mg, 26%); the characteristics of compounds **34** and **35** are given below.

(*R*)-(−)-6-Hydroxymethyl-5,5-dimethyltetrahydropyran-2-one 34. Mp 73–76 °C; $[a]_D^{19}$ −66.2 (*c* 2.55, $CHCl_3$); δ_H 0.92 (3 H, s, CMe^A), 1.02 (3 H, s, CMe^B), 1.59 (1 H, m, CH^ACMe_2), 1.70 (1 H, m, CH^BCMe_2), 2.52 (2 H, m, CH_2CO), 2.93 (1 H, br s, OH), 3.71 (2 H, m, CH_2O) and 4.09 (1 H, dd, *J* 7.1 and 3.4, CHO); δ_C 20.2, 26.3, 27.3, 30.8, 34.4, 61.7, 88.2 and 171.4; ν_{max}(Nujol mull)/cm^{-1} 3420, 1740, 1451 and 1060; *m*/*z* (APCI) 181 (M^+ + Na, 8%), 159 (M^+ + 1, 89), 141 (64) and 129 (100) (Found: C, 60.5; H, 9.2. $C_8H_{14}O_3$ requires C, 60.74; H, 8.92%). The enantiomeric purity was confirmed using the Chiralcel-OD column with detection at 233 nm [eluent: 10% isopropyl alcohol; t_R 10 (*R*) and 11 (*S*) min].

(*R*)-(−)-6-Acetoxymethyl-5,5-dimethyltetrahydropyran-2-one 35. Oil, $[a]_D^{19}$ −96.0 (*c* 1.06, $CHCl_3$); δ_H 0.98 (3 H, s, CMe^A), 1.07 (3 H, s, CMe^B), 1.61 (1 H, m, CH^ACMe_2), 1.73 (1 H, m, CH^B-CMe_2), 2.05 (3 H, s, Ac), 2.54 (2 H, m, CH_2CO), 4.05 (1 H, dd, *J* 12.0 and 8.1, CH^AOAc), 4.20 (1 H, dd, *J* 8.1 and 2.3, CH^BOAc), 4.31 (1 H, dd, *J* 12.0 and 2.3, CHO); δ_C 19.8, 20.6, 26.2, 27.0, 30.9, 34.3, 63.4, 84.4, 170.5 and 170.7; ν_{max} (liq. film)/cm^{-1} 1741, 1371, 1235 and 1040; *m*/*z* (EI) 200 (M^+, 3%), 126 (53), 70 (45), 56 (60) and 43 (100) (Found: C, 60.0; H, 8.3. $C_{10}H_{16}O_4$ requires C, 59.98; H, 8.05%). The enantiomeric purity was confirmed using the Chiralcel-OD column with detection at 233 nm [eluent: 10% isopropyl alcohol; t_R 13 (*R*) and 14 (*S*) min].

X-Ray crystallography

Data were collected on a Nicolet R3mV diffractometer at 20 °C using graphite-monochromated Mo-Kα radiation. Three standard reflections were monitored throughout the data collection and these showed no variation with time. The data were corrected for Lorentz and polarisation effects. The structures were solved by direct methods (SHELXS-86)[34] and developed using alternating cycles of least-squares refinement and difference-fourier synthesis (SHELXL-93).[35] Non-hydrogen atoms were refined anisotropically, while hydrogen atoms were placed in idealised positions and assigned a common isotropic thermal parameter.

Crystal data for 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-mannopyranose 20. $C_{14}H_{20}O_9S$, M = 364.4, monoclinic, space group $P2_1$, a = 9.701(2), b = 8.654(3), c = 11.331(3) Å, β = 97.76(3)°, V = 943 $Å^3$ (by least-squares refinement of diffractometer angles for 25 reflections in the range 16 < 2θ < 25°, λ = 0.710 73 Å), Z = 2, F(000) = 384, D_c = 1.28 g cm^{-3}, μ(Mo-Kα) = 2.12 cm^{-1}, plate 0.76 × 0.72 × 0.14 mm. Full matrix least-squares refinement on 218 parameters gave R = 0.0497 (R_w = 0.1198) for 1414 independent reflections [$I > 2\sigma(I)$] and R = 0.0721 (R_w = 0.1488) for all 1775 independent reflections in the range 5 ⩽ 2θ ⩽ 50°. The absolute configuration was determined using SHELXL-93 procedures [absolute structure parameter = 0.03(6)]. The final electron-density map was featureless with the largest peak 0.28 e $Å^{-3}$.‖

Crystal data for (*R*)-(−)-5,5-dimethyl-6-(triphenylsilylmethyl)tetrahydropyran-2-one 25. $C_{26}H_{28}O_2Si$, M = 400.6, orthorhombic, space group $P2_12_12_1$, a = 9.779(2), b = 11.404(2), c = 20.049(4) Å, V = 2236 $Å^3$ (by least-squares refinement of diffractometer angles for 17 reflections in the range 16 < 2θ < 24°, λ = 0.710 73 Å), Z = 4, F(000) = 856, D_c = 1.19 g cm^{-3}, μ(Mo-Kα) = 1.24 cm^{-1}, block 0.70 × 0.25 × 0.22 mm. Full matrix least-squares refinement on 262 parameters gave R = 0.0471 (R_w = 0.1178) for 2784 independent reflections [$I > 2\sigma(I)$] and R = 0.0626 (R_w = 0.1339) for all 3441 independent reflections in the range 5 ⩽ 2θ ⩽ 50°. The absolute configuration was determined using SHELXL-93 procedures [absolute structure parameter = −0.2(2)]. The final electron-density map was featureless with the largest peak 0.25 e $Å^{-3}$.‖

‖ Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/225.

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