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# Synthesis and characterization of homochiral cholesteryl 1-alkenesulfinate esters

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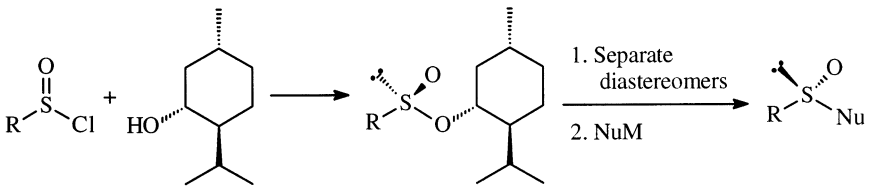
**Abstract**

A number of α,β-unsaturated sulfinyl chlorides **1** has been separately prepared and treated with (−)-cholesterol under various conditions some of which incorporated chiral amines quinine or quinidine. Some ($R_S$) vinylic sulfinates could be isolated in enantiopure form following one or two recrystallizations of the resulting diastereomeric mixtures of (−)-cholesteryl 1-alkenesulfinates **2**. Access to diastereomerically enriched ($S_S$) vinylic sulfinates (66–75% de) was achieved in three instances. Absolute stereochemical assignments were made with the assistance of the chiral solvating agent (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol. 

## 1. Introduction

Enantiopure sulfinate esters are an important class of organosulfur compounds. They are typically employed to prepare enantiopure or enantioenriched sulfoxides using various versions of the well-known Andersen methodology,[1] and the important role that enantiopure sulfoxides play in asymmetric synthesis is well documented.[2] The original Andersen procedure (Scheme 1) involves treating a sulfinyl chloride with (−)-menthol to generate a diastereomeric mixture of




Scheme 1.

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menthyl sulfinate esters which, following their separation, undergo organometallic substitution to afford enantiomerically pure sulfoxides.

Since the original Andersen method was first introduced several successful adaptations have been developed. These typically involve the use of other chiral alcohols such as diacetone-D-glucose (DAG),[3] (1*R*,2*S*)-(−)-*trans*-2-phenylcyclohexanol,[4] and cholesterol.[5] The use of DAG in combination with a specific choice of base and solvent has been found to be particularly successful with sulfinate de's sometimes exceeding 97%.[3] Since their introduction, enantiopure DAG sulfinates have proved particularly useful and have been employed as a source of chiral 2-sulfinyl thioacetamides,[6] alkylmethylthiomethyl sulfoxides[7] and *N*-sulfinylimines,[8] which in turn act as a source of other chiral species. The DAG alcohol has also recently been used for the kinetic resolution of bis-sulfinyl chlorides to synthesize $C_2$-symmetric bis-sulfinate esters.[9] Other chiral auxiliaries such as oxazolidinones[10] and Oppolzer's amide[11] have been found to serve as viable substitutes for chiral alcohols.

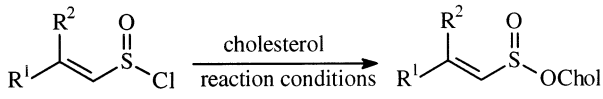
In many protocols targeting homochiral sulfinate esters, sulfinyl chlorides are used as the sulfur precursor.[12] Generally, the sulfinyl chlorides employed in this chemistry include Me, *p*-tolyl, *t*-Bu, and substituted aryl groups.[13] With a practical method established for the synthesis of 1-alkenesulfinyl chlorides[14] it was perceived that application of the Andersen methodology might provide a useful means for the preparation of homochiral α,β-unsaturated sulfinate esters. Our first success using 3,3-dimethyl-2-butenesulfinyl chloride was recently reported in communication form[15] and we describe herein the full results addressing the first synthesis of homochiral 1-alkenesulfinate esters.

## 2. Results and discussion

### 2.1. Synthesis of 1-alkenesulfinate esters

The initial experiments of the project were designed to examine a wide range of conditions to determine which sulfinate esters would provide optimal results. To accomplish this goal an array of small scale experiments was carried out in which a collection of α,β-unsaturated sulfinyl chlorides **1** were treated with $K_2CO_3$ and various chiral alcohols, chosen mostly on the basis of established synthetic procedures. These alcohols included: menthol, cholesterol, (DAG), (1*R*,2*S*)-(−)-*trans*-2-phenylcylcohexanol, borneol, and fenchyl alcohol. From these experiments three important pieces of information were gathered: (i) use of the established procedure for 1-alkenesulfinate formation[14] exhibited very little kinetic stereoselectivity; (ii) the diastereomers could not be separated using silica gel chromatography; and (iii) with the exception of cholesterol, all alcohols led to an oily, inseparable mixture of sulfinate diastereomers. On the basis of the information garnered, it was hoped that recrystallization of the cholesteryl sulfinates, which consistently presented themselves as a solid mixture of diastereomers, would provide access to enantiopure 1-alkenesulfinate esters.

Starting with the simplest system, larger scale reactions using ethenesulfinyl chloride **1a** were examined with cholesterol as the chiral auxiliary (Scheme 2). When $K_2CO_3$ was used as the base both low yields and de's of sulfinate **2a** were observed (Table 1, Entry 1).[16] The reproducibility of these results was also poor; possibly resulting from solubility problems encountered with the cholesterol/$K_2CO_3$ suspension at −78°C. Crystallization of the diastereomeric mixture did not result in any improvement to the de. Hence, various experiments using pyridine, $(i\text{Pr})_2\text{EtN}$ and




**1a-e** **2a-e**

Chol: (-)-cholesteryl

**a** $R^1$; $R^2$ = H; H, **b** $R^1$; $R^2$ = $CO_2Me$; H, **c** $R^1$; $R^2$ = *t*Bu; H,
**d** $R^1$; $R^2$ = Ph; H, **e** $R^1$; $R^2$ = Ph; Cl

Scheme 2.

Table 1
Preparation of homochiral cholesteryl 1-alkenesulfinate esters (Scheme 2)

| | Sulfinate product | | | Conditions[a] | | | Yield (%)/ de (%)[b] | Recrystallization[c] | |
|---|---|---|---|---|---|---|---|---|---|
| | # | $R^1$ | $R^2$ | Base | Temp. (°C) | Addition[d] | | De (%) | Yield (%) |
| 1 | **2a** | H | H | $K_2CO_3$ | −78 to −10 | A | 24/13 ($S_S$) | – | – |
| 2 | **2a** | H | H | Quinine | −78 | A | 51/35 ($R_S$) | 6 ($R_S$) | 3 |
| 3 | **2a** | H | H | Quinine | −78 to −20 | B | 57/47 ($R_S$) | – | – |
| 4 | **2a** | H | H | Quinidine | −78 | A | 49/25 ($S_S$) | 26 ($S_S$) | 6 |
| 5 | **2a** | H | H | Quinidine | −78 to −20 | B | 55/22 ($S_S$) | – | – |
| 6 | **2b** | $CO_2Me$ | H | $K_2CO_3$ | −78 to −20 | A | 63/56 ($R_S$) | 100 ($R_S$) | 26[e] |
| 7 | **2b** | $CO_2Me$ | H | Quinine | −78 to −20 | B | 89/6 ($S_S$) | 86 ($R_S$) | 20 |
| 8 | **2b** | $CO_2Me$ | H | Quinidine | −78 to −20 | B | 80/12 ($R_S$) | 64 ($R_S$) (100 ($R_S$)) | 38 (27) |
| 9 | **2c** | *t*Bu | H | $K_2CO_3$ | −78 to −20 | A | 42/0 | 86 ($R_S$) (100 ($R_S$)) | 20 (8) |
| 10 | **2c** | *t*Bu | H | $K_2CO_3$ | −78 to rt | B | 53/4 ($R_S$) | 92 ($R_S$) | 20 |
| 11 | **2c** | *t*Bu | H | Quinine | −78 to −20 | B | 76/50 ($R_S$) | 95 ($R_S$) | 32 |
| 12 | **2c** | *t*Bu | H | Quinine | −78 to rt | B | 83/39 ($R_S$) | 95 ($R_S$) (100 ($R_S$)) | 42 (36) |
| 13 | **2c** | *t*Bu | H | Quinidine | −78 | B | 94/65 ($S_S$) | 68 ($S_S$) | 46[f] |
| 14 | **2c** | *t*Bu | H | Quinidine | −78 to −20 | B | 82/63 ($S_S$) | 70 ($S_S$) (75 ($S_S$)) | 31[f] (12)[f] |
| 15 | **2d** | Ph | H | $K_2CO_3$ | −78 to −20 | B | 48/3 ($S_S$) | 100 ($R_S$) | 8 |
| 16 | **2d** | Ph | H | Quinine | −78 to −20 | B | 73/43 ($R_S$) | 100 ($R_S$) | 21 |
| 17 | **2d** | Ph | H | Quinidine | −78 to −20 | B | 82/43 ($S_S$) | 86 ($R_S$) | 14 |
| 18 | **2e** | Ph | Cl | Quinine | −78 to rt | B | 88/10 ($R_S$) | 52 ($S_S$)[f] (94 ($S_S$))[f] | 23 (12) |
| 19 | **2e** | Ph | Cl | Quinidine | −78 to rt | B | 89/9 ($S_S$) | 82 ($S_S$)[f] | 11 |

[a] Solvent was $CH_2Cl_2$ unless otherwise noted.
[b] Sulfinate **2** was obtained as a mixture of diastereomers; de refers to initial de after chromatography.
[c] Values in parentheses refer to a second recrystallization; crystallization solvent was hexanes unless otherwise noted.
[d] Addition mode A: alcohol and base added to sulfinyl chloride solution; addition mode B: sulfinyl chloride solution added to alcohol and base solution.
[e] An overall yield of 39% was observed after additional recrystallizations of the mother liquor.
[f] Recrystallized from acetone.

sparteine were carried out under several different temperature and solvent conditions in an attempt to optimize both the yield and de of the cholesteryl ethenesulfinate. Unlike the DAG methodology[3] the achiral amine bases did not afford high yields nor high stereoselectivity. It was suggested, based upon the work reported by Mikolajczyk and co-workers,[17] that switching to

chiral amines such as quinine and quinidine might provide a means to improving both yields and de's.

Using the chiral amine base, sulfinyl chloride **1a** was again treated with cholesterol to afford sulfinate **2a** (Table 1, Entries 2–4). Under these conditions improvements to both the yield and de, and moreover, access to either sulfur epimer were achieved. Again, in an effort to achieve higher de's and yields, various conditions were manipulated including temperature, solvent and mode of addition of the reactants. The best yields and de's were achieved using $CH_2Cl_2$ as the solvent, increasing and then holding the temperature from −78 to −20°C until completion of the reaction and finally, transferring the crude sulfinyl chloride solution to a pre-cooled solution of cholesterol and base (Table 1, addition mode B). Unfortunately, all attempts to isolate either sulfur epimer in an enantiopure form through recrystallization met with little success.

Application of the quinine or quinidine methodology to sulfinyl chlorides **1b–e** offered improved yields of sulfinates **2b–e**, with low to moderate de's.[18] More importantly, enantiopure ($R_S$) versions of sulfinates **2b–d** were obtained after one or two crystallizations from hexanes.[19] For sulfinate **2b**, regardless of the isomeric enrichment, preferential crystallization of the ($R_S$) isomer was observed. In the case of sulfinate **2e**, preferential crystallization of the ($S_S$) was observed following one to two crystallizations from hexanes. Access to ($S_S$)-**2b** was achieved as follows. Once exhaustive recrystallizations of ($R_S$) has been performed, the mother liquor, now enriched in the ($S_S$) isomer, was concentrated to afford ($S_S$)-**2b** (66% de). A single recrystallization of the ($S_S$)-**2c** reaction mixture from acetone provided that material in 70% de. Unfortunately, neither procedure was generally applicable to other substrates.[20]

The first significant kinetic selectivity found in the formation of enantioenriched sulfinic esters was by Alcudia et al using the DAG sulfinates.[3a] Those authors offer a speculative mechanism whereby an amine base reacts with the sulfinyl chloride to generate a racemic pair of sulfinyl ammonium diastereomers, which then react with the chiral alcohol to afford sulfurane intermediates. Those sulfuranes may or may not undergo pseudorotations prior to releasing the enantiopure sulfinate. The selectivity is believed to arise through differences in stability between the sulfurane intermediates. The complexity of their suggested mechanism coupled with unanswered questions concerning the behavior of their proposed sulfuranes precludes us from applying their mechanism to our compounds. Further, the de's of the sulfinates formed in this work are comparatively lower and hence we are in no position at this time to account for the observed diastereoselectivity in the formation of sulfinates **2**.

### *2.2. Determination of enantiopurity and absolute configuration of 1-alkenesulfinate esters*

The diastereomeric excesses of the vinylic sulfinates were determined using $^1$H NMR spectroscopy in $C_6D_6$.[21] An examination of the vinyl hydrogen peaks indicated the presence of two isomers, with chemical shift differences between the two peaks sufficient to accurately measure the de (Fig. 1a,b). Assignment of the absolute configuration was achieved using the chiral solvating agent ($R_S$)-2,2,2-trifluoro-1-(9-anthryl)ethanol **3**. Using a model proposed by Pirkle[22] involving two hydrogen bonding interactions (Fig. 2), the chemical shifts of the vinyl hydrogens can be correlated to the absolute configuration. In complex A the vinyl hydrogens are shielded by the anthryl group resulting in an upfield shift. Conversely, in complex B no shielding of the

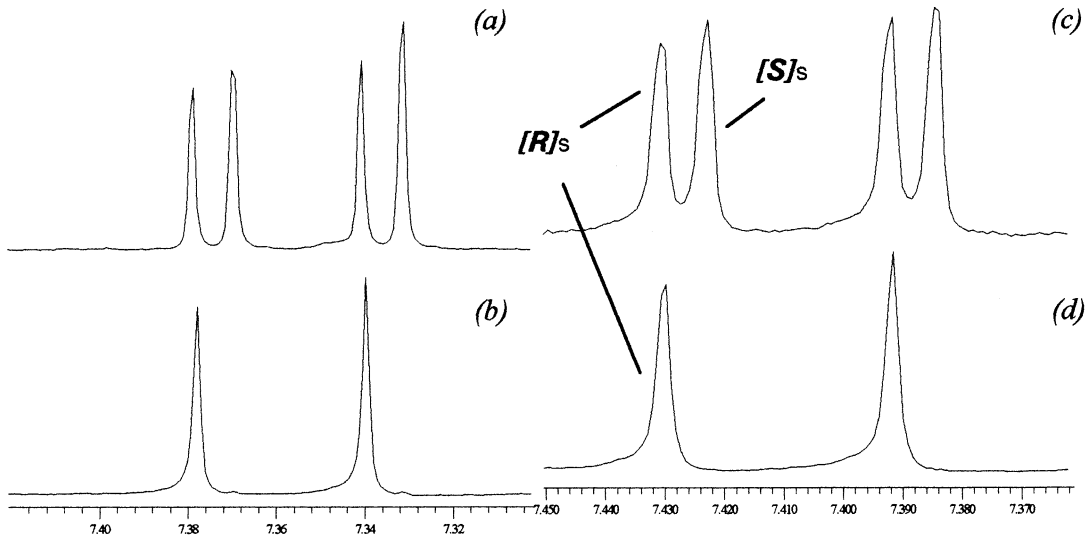



Figure 1. Spectrum for α-vinyl hydrogen ($H_a$) peaks for sulfinate **2b** as (a) mixture of two isomers in $C_6D_6$; (b) isolated enantiopure in $C_6D_6$; (c) two isomers with 1 equiv. of **3**; and (d) enantiopure with 1 equiv. of **3**

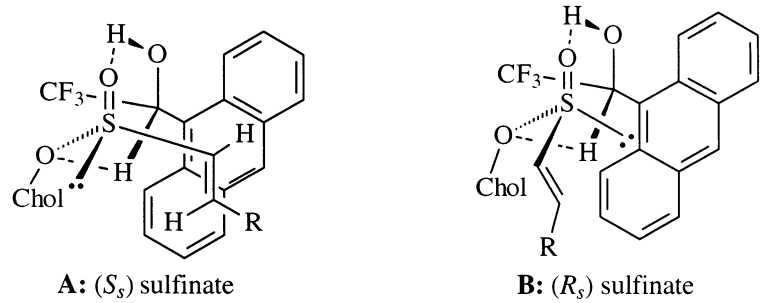



Figure 2. Differential shielding effects of CSA **3** on a vinylic sulfinate

vinyl hydrogens is anticipated and hence the hydrogen resonance remain comparatively downfield. On this basis the upfield diastereomeric peak represents the ($S_S$) isomer while the downfield peak represents the ($R_S$) isomer (Fig. 1c,d).

To support further our configurational assignments of **2c**, the circular dichroism (CD) spectra were obtained for both isomers and their Cotton effects (CE) analyzed. The CD curves shown in Fig. 3 are representative of ($R_S$) and ($S_S$)-**2c**. For ($R_S$)-**2c** (Fig. 3a) there is a slight positive CE around 278 nm followed by a strongly negative CE around 254 nm. This strong CE corresponds to the $\lambda_{max}$ of 252.0 nm obtained from the UV absorption spectrum of **2c**. The CD spectrum of ($S_S$)-**2c** (Fig. 3b) exhibits a slight negative CE followed by a strong CE around 254 nm. As the ($S_S$) isomer is enriched (70% de) and the ($R_S$) isomer is enantiopure the intensity of the CE for ($S_S$)-**2c** is not as great. Notice also that the two curves in Fig. 3 are mirror images of each other, confirming their opposite configurations at sulfur.[23]

To conclude, the first preparation of enantiopure α,β-unsaturated esters has been achieved. The capture of 1-alkenesulfinyl chlorides with (−)-cholesterol in the presence of quinine or quinidine affords the corresponding cholesteryl 1-alkenesulfinate esters with de's $\leq$63%. Follow-

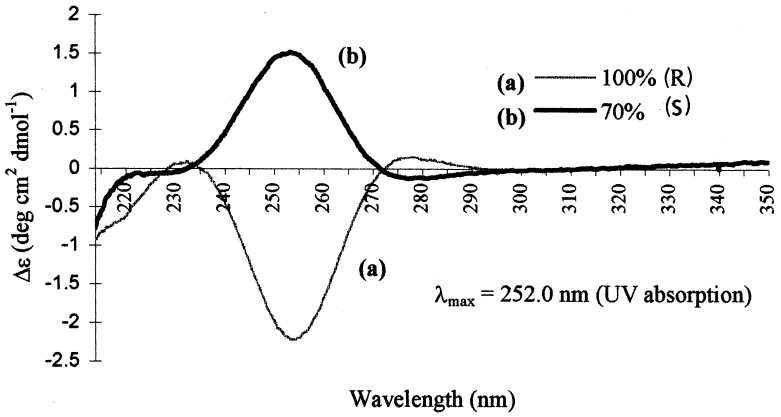



Fig. 3. Circular dichroism curves for (a) ($R_S$)-**2c**; (b) ($S_S$)-**2c**

ing one or two recrystallizations the α,β-unsaturated sulfinate esters can be isolated in enantioenriched or enantiopure form. The yields obtained are significantly greater than those reported for the cholesterol capture of alkane- or arenesulfinyl chlorides,[5] where (−)-cholesterol has been employed previously. Nucleophilic substitution reactions of the various 1-alkenesulfinate esters **2** and the anticipated formation of enantioenriched 1-alkenyl sulfoxides is currently under investigation.

## 3. Experimental

### 3.1. General

Melting points are uncorrected. Infrared (IR) spectra were obtained on a Bomen FTIR spectrometer in a solution cell ($CH_2Cl_2$ or $CDCl_3$). NMR spectra for $^1H$ and $^{13}C$ NMR were recorded at 400 and 100.6 MHz, respectively, in $CDCl_3$ and $C_6D_6$ (for enantiopure or enantioenriched sulfinates). Mass spectra (MS) were obtained using chemical ionization and electron impact techniques. CD spectra were recorded on a Jasco J-600 spectropolarimeter. Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium and benzophenone. Methylene chloride, pyridine and ($i$-Pr)$_2$EtN were distilled from calcium hydride. Air and water sensitive reagents were transferred via oven-dried nitrogen-purged syringes. Flash chromatography was performed on virgin 200–425 mesh Type 60 Å silica gel. Analytical thin-layer chromatography (TLC) was performed using 0.25 mm Merck Kieselgel 60 F254 precoated silica gel plates. Sulfuryl chloride was purchased from Aldrich as a 1.0 M solution in $CH_2Cl_2$. Older solutions were discarded before complete consumption of their contents. Elemental analyses were performed by MHW Labs of Phoenix, AZ. With one exception,[24] the preparations of the starting sulfoxides have been reported previously.[14]

### 3.2. General method for the oxidative fragmentation of 1-alkenyl (DPM or PMB) sulfoxides and capture as cholesteryl 1-alkenesulfinate esters

To a solution of 1-alkenyl diphenylmethyl (DPM; or $p$-methoxybenzyl (PMB)) sulfoxide (1.0 equiv.) in dry $CH_2Cl_2$ (5 mL/mmol) at −78°C under $N_2$ was added $SO_2Cl_2$ (1.1–1.3 equiv., as a 1 M solution in $CH_2Cl_2$) via syringe. The mixture was stirred for 10 minutes then allowed to

warm to room temperature over 1 hour. After recooling to −78°C and stirring for 10 minutes. the sulfinyl chloride solution was transferred via syringe to a −78°C solution of cholesterol and base in $CH_2Cl_2$ (7.5 mL/mmol). The reaction mixture was allowed to warm slowly to −20°C and stirred overnight. When complete by TLC analysis, the reaction mixture was concentrated under reduced pressure. The vinylic sulfinate product was then isolated using silica gel flash chromatography with EtOAc/hexanes as the eluent. Sulfinate ester yields were calculated from the amount of cholesterol added.

*3.2.1. Synthesis of cholesteryl ($R_S$)-ethenesulfinate* ***2a***

The reaction of DPM ethenyl sulfoxide (700 mg, 2.89 mmol) with $SO_2Cl_2$ (3.76 mL, 3.76 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (950 mg, 2.46 mmol) and quinine (1.13 g, 3.47 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to −20°C and stirred overnight. Diastereomerically enriched sulfinate **2a** (650 mg, 57%, 42% $[R]_S$) was isolated as a solid after flash chromatography (two columns, 10% EtOAc/hexanes). Mp (diastereomerically enriched ($R_S$) sulfinate): 83–84°C; $[\alpha]_D^{25}$: −26.3 (*c* 2.16, acetone). $^1$H NMR (400 MHz) $\delta$: 6.67 (dd, $J=16.8$ and 10.0 Hz, 1H), 6.11 (d, $J=16.8$ Hz, 1H), 5.94 (d, $J=10.0$ Hz, 1H), 5.37 (m 1H), 4.15 (m, 1H), 2.47–2.41 (m, 2H), 1.00 (s, 3H), 0.90 (d, $J=6.5$ Hz, 3H), 0.85 (d, $J=6.6$ Hz, 3H), 0.85 (d, $J=6.6$ Hz. 3H), 0.66 (s, 3H), 2.01–1.03 (m, remaining peaks for cholesteryl skeleton, 26H); $^{13}$C NMR (100.6 MHz) $\delta$: 143.6, 139.4, 123.9, 123.0, 79.4, 56.6, 56.1, 49.9, 42.2, 40.2 (40.1), 39.6, 39.5, 37.1 (37.1), 36.4, 36.1, 35.7, 31.8, 31.8, 29.9 (29.7), 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.0, 19.2, 18.7, 11.8 (bracketed values are representative of the ($S_S$) isomer); IR ($CH_2Cl_2$) cm$^{-1}$: 2930, 2907, 2868, 2855, 1606, 1468, 1382, 1375, 1368, 1127, 1027, 1005, 970, 946; MS (CI, $NH_3$) *m/z* (%): 386 (33), 370 (24), 369 (87), 368 (100). Anal. calcd for $C_{29}H_{48}O_2S$: C, 75.60; H, 10.50. Found: C, 75.54; H, 10.35.

*3.2.2. Synthesis of cholesteryl ($S_S$)-ethenesulfinate* ***2a***

The reaction of DPM ethenyl sulfoxide (976 mg, 4.03 mmol) with $SO_2Cl_2$ (5.24 mL, 5.24 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (1.33 g, 3.43 mmol) and quinidine (1.57 g, 4.84 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to −20°C and stirred overnight. Diastereomerically enriched sulfinate **2a** (658 mg, 42%, 17% ($S_S$) was isolated as a solid after flash chromatography (two columns, 10% EtOAc/hexanes). Mp (diastereomerically enriched ($S_S$) sulfinate): 81–83°C; $[\alpha]_D^{25}$: −18.2 (*c* 2.42, acetone).

*3.2.3. Synthesis of cholesteryl ($R_S$)-(E)-2-carbomethoxyethenesulfinate* ***2b***

The reaction of PMB (*E*)-2-carbomethoxyethenyl sulfoxide (721 mg, 2.84 mmol) with $SO_2Cl_2$ (3.69 mL, 3.69 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (933 mg, 2.41 mmol) and quinidine (1.11 g, 3.41 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to −20°C and stirred for several hours. Diastereomerically enriched sulfinate **2b** (1.01 g, 81%, 12% ($R_S$)) was isolated as a solid after flash chromatography (3–5% EtOAc/hexanes). Following crystallization from hexanes the ($R_S$) sulfinate was isolated in a 38% yield (64% ($R_S$)). Following a second crystallization from hexanes the enantiopure ($R_S$) sulfinate was obtained in a 27% yield. Mp (enantiopure ($R_S$) sulfinate): 130–132°C; $[\alpha]_D^{25}$: −25.6 (*c* 1.06, acetone). $^1$H NMR (400 MHz) $\delta$: 7.44 (d, $J=15.4$ Hz, 1H), 6.61 (d, $J=15.4$ Hz, 1H), 5.38 (m, 1H), 4.81 (m, 1H), 3.82 (s, 3H), 2.42 (m, 2H), 1.00 (s, 3H), 0.91 (d, $J=6.4$ Hz, 3H), 0.86 (d, $J=6.4$ Hz, 3H), 0.85 (d, $J=6.8$ Hz, 3H), 0.67 (s, 3H), 2.05–0.85 (m, remaining peaks for cholesteryl skeleton, 26H); $^{13}$C NMR (100.6 MHz) $\delta$: 164.3, 149.7, 139.1, 128.0, 123.3, 80.6,

56.6, 56.1, 52.5, 49.9, 42.3, 40.1, 39.7, 39.5, 37.0, 36.4, 36.1, 35.7, 31.8, 31.8, 29.8, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 19.3, 18.7, 12.5; IR ($CDCl_3$) $cm^{-1}$: 3054, 2953, 2865, 1729, 1617, 1467, 1439, 1384, 1371, 1294, 1269, 1222, 1137, 1120, 1027, 994, 971; MS (CI, $NH_3$) $m/z$ (%): 386 (23), 371 (29), 370 (100), 368 (19), 135 (12), 119 (11), 103 (23), 87 (13), 65 (18). Anal. calcd for $C_{31}H_{50}O_4S$: C, 71.77; H, 9.71. Found: C, 71.50; H, 9.48.

*3.2.4. Synthesis of cholesteryl ($S_S$)-(E)-2-carbomethoxyethenesulfinate* ***2b***

After multiple crystallizations from hexanes the ($S_S$) sulfinate was isolated diastereomerically enriched (66% de). Mp (diastereomerically enriched ($S_S$) sulfinate): 108–110°C; $[\alpha]_D^{25}$: −11.8 (*c* 1.36, acetone).

*3.2.5. Synthesis of cholesteryl ($R_S$)-(E)-3,3-dimethylbutenesulfinate* ***2c***

The reaction of DPM (*E*)-(3,3-dimethyl-1-butenyl) sulfoxide (1.12 g, 3.75 mmol) with $SO_2Cl_2$ (4.9 mL, 4.88 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (1.24 g, 3.19 mmol) and quinine (1.22 g, 3.75 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to rt and stirred overnight. Diastereomerically enriched sulfinate **2c** (1.36 g, 83%, 39% de ($R_S$)) was isolated as a solid after flash chromatography (3–5% EtOAc/hexanes). Following crystallization from hexanes, the enantiopure ($R_S$) sulfinate was isolated in a 42% yield (89% ($R_S$)). Following a second crystallization from hexanes the ($R_S$) sulfinate was obtained diastereomerically pure in a 36% yield. Mp (enantiopure ($R_S$) sulfinate): 153–154°C; $[\alpha]_D^{25}$: −23.2 (*c* 1.33, $CHCl_3$). $^1H$ NMR (400 MHz): $\delta$: 6.48 (d, $J=15.7$ Hz, 1H), 6.22 (d, $J=15.7$ Hz, 1H), 5.37 (m, 1H), 4.14 (m, 1H), 2.48–2.41 (m, 2H), 1.10 (s, 9H), 1.01 (s, 3H), 0.91 (d, $J=6.5$ Hz, 3H), 0.87 (d, $J=6.6$ Hz, 3H), 0.86 (d, $J=6.6$ Hz, 3H), 0.67 (s, 3H), 0.85–2.02 (remaining peaks for cholesteryl skeleton, 26H); $^{13}C$ NMR (100.6 MHz) $\delta$: 152.0, 139.6, 131.8, 122.8, 78.7, 56.6, 56.1, 49.9, 42.3, 40.3, 39.7, 39.5, 37.2, 36.5, 36.2, 35.8, 34.0, 31.9, 31.8, 29.7, 28.7, 28.2, 28.0, 24.3, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8; IR ($CH_2Cl_2$) $cm^{-1}$: 3041, 2944, 2898, 1667, 1623, 1465, 1367, 1129, 1115, 996, 976; MS (CI, $NH_3$) $m/z$ (%): 516 ($M^+$, 1), 386 (8), 371 (29), 370 (100), 369 (7), 368 (22), 354 (7), 149 (10), 133 (8), 131 (5), 115 (8), 83 (2), 57 (12). Anal. calcd for: $C_{33}H_{56}O_2S$: C, 76.68; H, 10.92. Found: C, 76.85; H, 10.68.

*3.2.6. Synthesis of cholesteryl ($S_S$)-(E)-3,3-dimethylbutenesulfinate* ***2c***

The reaction of DPM (*E*)-(3,3-dimethyl-1-butenyl) sulfoxide (902 mg, 3.03 mmol) with $SO_2Cl_2$ (3.63 mL, 3.63 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (994 mg, 2.57 mmol) and quinidine (1.18 g, 3.63 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to −20°C and stirred overnight. Diastereomerically enriched sulfinate **2c** (1.19 g, 82%, 63% de ($S_S$)) was isolated as a solid after flash chromatography (3–5% EtOAc/hexanes). Following crystallization from acetone the ($S_S$) sulfinate was isolated in a 31% yield (70% ($S_S$)). Following a second crystallization from acetone the diastereomerically enriched ($S_S$) sulfinate was isolated in a 12% yield (75% de ($S_S$)). Mp (diastereomerically enriched 70% ($S_S$)): 130–132°C; $[\alpha]_D^{25}$: −16.6 (*c* 1.14, $CHCl_3$).

*3.2.7. Synthesis of cholesteryl ($R_S$)-(E)-2-phenylethenesulfinate* ***2d***

The reaction of DPM (*E*)-2-phenylethenyl sulfoxide (457 mg, 1.68 mmol) with $SO_2Cl_2$ (2.02 mL, 2.02 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (552 mg, 1.43 mmol) and quinine (654 mg, 2.02 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to −20°C and stirred overnight. Diastereomerically enriched sulfinate **2d** (562 mg, 73%,

43% ($R_S$)) was isolated as a solid after flash chromatography (3–5% EtOAc/hexanes). Following crystallization from hexanes the enantiopure ($R_S$) sulfinate was isolated in a 21% yield (100% ($R_S$)). Mp (enantiopure ($R_S$) sulfinate): 158–160°C; $[\alpha]_D^{25}$: +14.3 (*c* 2.65, $CHCl_3$). $^1H$ NMR (400 MHz) $\delta$: 7.51–7.49 (m, 2H), 7.42–7.38 (m, 3H), 7.27 (d, $J=16.0$ Hz, 1H), 6.92 (d, $J=16.0$ Hz, 1H), 5.37 (m, 1H), 4.21 (m, 1H), 2.51–2.45 (m, 2H), 1.01 (s, 3H), 0.91 (d, $J=6.6$ Hz, 3H), 0.87 (d, $J=6.6$ Hz, 3H), 0.86 (d, $J=6.6$ Hz, 3H), 0.67 (s, 3H), 2.02–1.03 (m, remaining peaks for cholesteryl skeleton, 26H); $^{13}C$ NMR (100.6 MHz) $\delta$: 139.5, 138.5, 133.4, 133.2, 130.2, 218.9, 128.0, 123.0, 56.6, 56.1, 49.9, 42.3, 39.7, 39.5, 37.1, 36.5, 36.1, 35.8, 31.9, 31.8, 29.8, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.0, 19.2, 18.7, 11.8; IR ($CH_2Cl_2$) $cm^{-1}$: 3050, 2911, 2909, 2869, 2855, 1614, 1124, 973, 946; MS (EI) *m/z* (%): 369 (2), 119 (12), 118 (24), 91 (38), 79 (16), 76 (13), 59 (38), 58 (62), 43 (100), 42 (15); MS (positive ion ESI): 537. Anal. calcd for $C_{35}H_{52}O_2S$: C, 78.30; H, 9.76. Found: C, 78.19; H, 9.53.

*3.2.8. Synthesis of cholesteryl ($S_S$)-(Z)-2-chloro-2-phenylethenesulfinate* ***2e***

The reaction of (*Z*)-2-chloro-2-phenylethenyl-2-(trimethylsilyl)ethyl sulfoxide[24] (551 mg, 1.92 mmol) with $SO_2Cl_2$ (2.31 mL, 2.31 mmol) yielded sulfinyl chloride, which was transferred to a solution of cholesterol (632 mg, 1.63 mmol) and quinidine (749 mg, 2.31 mmol) in $CH_2Cl_2$ at −78°C. The reaction mixture was warmed to rt and stirred overnight. Diastereomerically enriched sulfinate **2e** (823 mg, 88%, 10% ($R_S$)) was isolated as a solid after flash chromatography (3–5% EtOAc/hexanes). Following crystallization from hexanes the ($S_S$) sulfinate was isolated in a 23% yield (52% ($S_S$)). Following a second crystallization from hexanes the diastereomerically enriched ($S_S$) sulfinate was isolated in a 12% yield (94% ($S_S$)). Mp (diastereomerically enriched ($S_S$) sulfinate): 141–142°C; $[\alpha]_D^{25}$: −43.6 (*c* 2.22, $CHCl_3$). $^1H$ NMR (400 MHz) $\delta$: 7.47–7.43 (m, 3H), 7.42–7.37 (m, 2H), 7.14 (s, 1H), 5.27 (m, 1H), 4.06 (m, 1H), 0.93 (s, 3H), 0.90 (d, $J=6.8$ Hz, 3H), 0.86 (d, $J=6.4$ Hz, 3H), 0.86 (d, $J=6.8$ Hz, 3H), 0.65 (s, 3H), 2.20–0.69 (m, remaining peaks for cholesteryl skeleton, 28H); $^{13}C$ NMR (100.6 MHz) $\delta$: 147.9, 139.2, 129.7, 129.2, 128.9, 126.6, 123.0, 80.5, 56.6, 56.0, 49.8, 42.2, 39.7, 39.6, 39.4, 37.0, 36.4, 36.1, 35.7, 31.8, 31.7, 29.6, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 20.9, 19.1, 18.7, 11.8; IR ($CH_2Cl_2$) $cm^{-1}$: 3062, 2943, 2868, 2852, 1490, 1467, 1444, 1382, 1367, 1136, 992. Anal. calcd for $C_{35}H_{51}ClSO_2$: C, 73.58; H, 9.00. Found: C, 73.63; H, 8.88.

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19. Further crystallizations of the recovered mother liquor offered improvements of up to 15% for the overall recovery of the enantiopure sulfinate esters.
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24. The procedure used to prepare this starting sulfoxide will be published elsewhere. See: Schwan, A. L.; Strickler, R. R.; Dunn-Dufault, R.; Brillon, D. *Eur. J. Org. Chem*., in press.