Uncatalysed (thermal) and Lewis acid-promoted asymmetric hetero-Diels–Alder reaction of 1-thiabuta-1,3-dienes (thiochalcones) with di-(−)-menthyl fumarate. Configuration determination by X-ray crystallographic analysis of (2*S*,3*R*,4*R*)-(+)-2,3-bis[(−)-menthoxycarbonyl]-4,6-diphenyl-3,4-dihydro-2*H*-thiopyran and conversion of cycloadducts into optically pure diols

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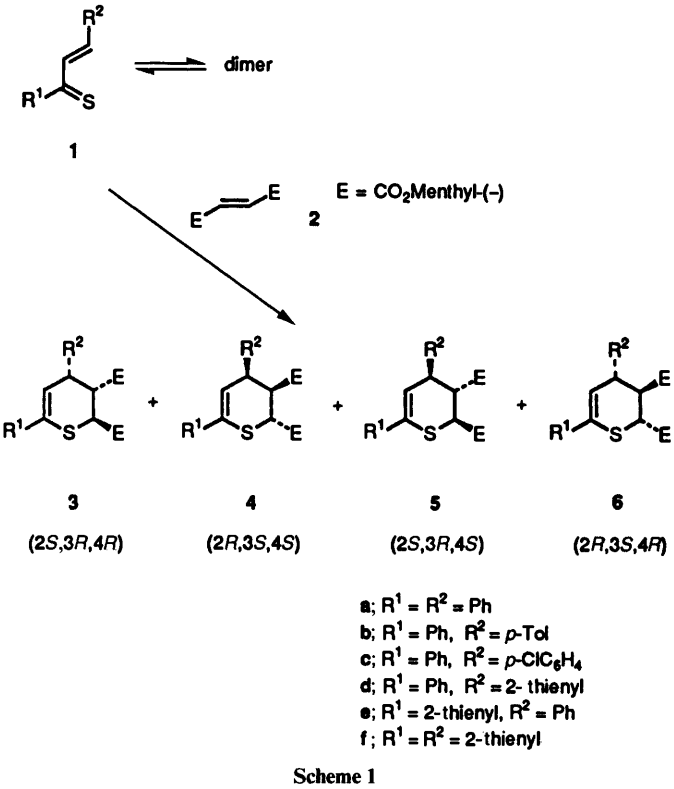
1-Thiabuta-1,3-dienes 1 (thiochalcones) underwent asymmetric hetero-Diels–Alder reaction with di-(−)-menthyl fumarate 2 to afford a mixture of 3,4-*cis*- (3 and 4) and 3,4-*trans*-dihydrothiopyrans (5 and 6) in good-to-excellent chemical yield with fair diastereoselectivities, the stereoisomer 3 predominating. An *endo* (3,4-*cis*):*exo* (3,4-*trans*) selectivity was observed in the ratio 98–85:2–15. The uncatalysed reaction at 20–40 °C showed 10–48% de in diastereo-π-facial selectivity, while the selectivity was improved to 62–71% de by using a suitable Lewis acid under appropriate reaction conditions. The 3,4-*cis*-stereoisomer formed favourably in both thermal and Lewis acid-promoted reactions, had the same configuration 2*S*,3*R*,4*R* (3). The configuration was unequivocally established by X-ray crystallographic structural analysis using the isomer 3a (R^1 = R^2 = Ph). The isomer 3, which could be obtained stereochemically homogeneous by chromatography and recrystallization, was consecutively transformed to optically pure diols 7 and 8 or 9 by $LiAlH_4$ reduction, followed by reductive desulfurization with Raney Ni.

Introduction

Asymmetric Diels–Alder reaction has been one of the most powerful and important methods for regio- and stereo-selective synthesis of substituted cyclohexenes, which can be converted into useful chiral intermediates, and an enormous amount of work has been devoted to its development.[1] In recent years, its versatility has increasingly become apparent also in a variant of asymmetric hetero-Diels–Alder (AHDA) reaction.[2–4] In spite of its promising, high potential in asymmetric heterocycle synthesis, however, the use of heteroatom cycloaddends has been limited, in most cases, to only oxa- and aza-dienes or -dienophiles; only a few examples of thia-AHDA reactions have been reported so far.[3] Recently Vedejs *et al.*, Kirby and Sclare, Koizumi *et al.* and Bonini *et al.* reported AHDA reactions in which thioaldehydes[5,6] and a silyl thioketone[7] participated as heterodienophiles. Zwanenburg and co-workers showed that chiral sulfines (thiocarbonyl *S*-oxides) reacted as heterodienophiles on the configurationally rigid C=S bond.[8] Also, chiral *N*-sulfinylamines acted as thia-dienophiles on the N=S bond in an AHDA reaction.[9] However, there had been no precedent until our previous preliminary report of a 1-thiabuta-1,3-diene system taking part as heterodiene in an AHDA reaction.[10,11] Furthermore, we have revealed that some suitable Lewis acids can be utilized as efficient promoters in this AHDA reaction. Here we describe the results with full experimental details of this research including conversion of cycloadducts to optically active organic compounds as well as configurational determination by means of X-ray crystallographic analysis.



Scheme 1

Results and discussion

Thermal AHDA reaction

Thiochalcones **1**, which could be thermally generated at a proper temperature from its dimer, reacted with di-(−)-menthyl fumarate **2** to afford a cycloadduct in nearly quantitative yield (Table 1). The cycloadduct was found to be a

Table 1 Uncatalysed (thermal) asymmetric hetero-Diels–Alder reaction of thiabutadiene **1** with di-(−)-menthyl furnarate **2**

Run[a]	Thioketone[b]	Solvent	Time (*t*/*h*)	Cycloadduct	Yield (%)[c]	Ratio of *endo* isomers **3**:**4** (% de)[d,e]
1	**1a**	CH_2Cl_2	25	**3a–6a**	99	64:36 (28)
2[f]	**1a**	CH_2Cl_2	11 d	**3a–6a**	93	67.5:32.5 (35)
3	**1a**	CCl_4	25	**3a–6a**	92	61:39 (22)
4[g]	**1a**	Et_2O	36	**3a–6a**	94	59.5:40.5 (19)
5	**1a**	Benzene	25	**3a–6a**	82	55:45 (10)
6	**1a**	Toluene	26	**3a–6a**	92	58:42 (16)
7	**1a**	$CHCl_3$	25	**3a–6a**	95	74:26 (48)
8	**1b**	CH_2Cl_2	20	**3b–6b**	98	63:37 (26)
9	**1b**	CCl_4	22	**3b–6b**	99	58:42 (16)
10	**1b**	Toluene	21	**3b–6b**	83	55:45 (10)
11	**1b**	$CHCl_3$	23	**3b–6b**	86	70:30 (40)
12	**1c**	CH_2Cl_2	28	**3c–6c**	96	59:41 (18)
13	**1c**	CCl_4	28	**3c–6c**	89	62:38 (24)
14	**1c**	Toluene	29	**3c–6c**	94	57:43 (14)
15	**1c**	$CHCl_3$	27	**3c–6c**	93	65:35 (30)
16	**1d**	$CHCl_3$	8 d	**3d–6d**	91	65:35 (30)
17	**1e**	$CHCl_3$	8 d	**3e–6e**	95	65:35 (30)
18	**1f**	$CHCl_3$	15 d	**3f–6f**	97	65:35 (30)

[a] The reactions were carried out at 40 °C in a molar ratio of **1**:**2** = 1:1.2 unless otherwise noted. [b] Dithiine-type dimers **D** were used for **1a–c** and thiopyran-type dimers **T** for **1d–f**.‡ [c] Isolated total yield of diastereoisomers. [d] Ratios of *endo*-(**3** + **4**): *exo*-isomers (**5** + **6**) were observed >98:2 for **1a,b**, 85:15 ± 4 for **1c** and 95:5 ± 1 for **1d–f**. [e] Determined by HPLC analysis and ^1H NMR (270 or 500 MHz) spectroscopy. [f] At 20 °C. [g] At 35 °C. ‡ See footnote in text.

mixture of four possible diastereoisomers, *viz.* two 3,4-*cis*(*endo*)- (**3** and **4**) and two 3,4-*trans*(*exo*)-isomers (**5** and **6**),† in the ratio *cis*:*trans* = 98–85:2–15, as determined by HPLC and/or ^1H NMR spectroscopy. The ratio of the major *cis*-adducts (**3**:**4**) related to diastereo-π-facial differentiation selectivity (de) was variable and depended upon the solvents and temperatures employed. Uncatalysed reactions at ≪40 °C were impractically slow (*e.g.*, Run 2), probably owing to inefficiency of the thermal dissociation of dimers,[12] whilst reactions at higher temperatures proceeded more quickly but lowered the π-facial selectivity. The best de-values for substrates **1a–f** were obtained when the reaction was carried out in chloroform (Runs 7, 11 and 15–18; 48% for **1a**, 40% for **1b** and 30% for **1c–f**). The precursor dimer structures (dithiin type **D** and thiopyran type T) employed in this reaction indeed affected the reaction rates (Runs 1–15 *versus* 16–18). This is consistent with our previous observation that dimer **D** is a kinetically favoured product, that both dimers are in equilibrium at adequate temperatures, and that thermodynamically more stable dimer T considerably more slowly dissociates than does dimer **D**.‡[,12] However, very little was observed to have an influence on de-values upon alteration of the dimers **D** and T of **1a**, as shown in Fig. 1. Furthermore, neither isomerization of the cycloadducts **3–6** nor conspicuous deviation of de-values (Δ de% < ±2) during the reaction was observed, suggesting that the cycloadducts are stable under the reaction conditions and hence are kinetically controlled products.

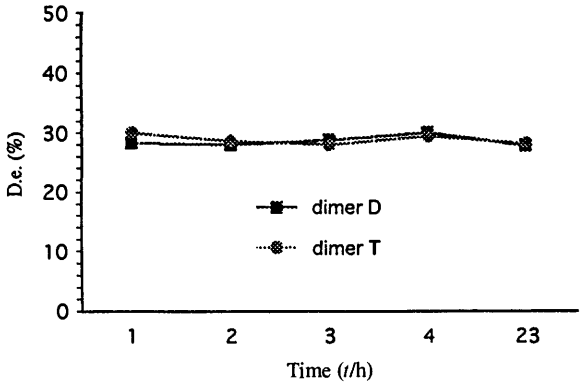
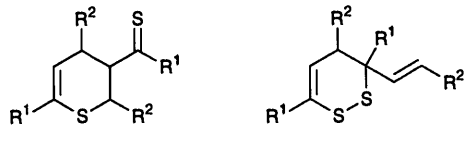


Fig. 1 De plots of the *cis*-cycloadducts (**3a**, **4a**) on reaction time for the reaction using dimers **D** and **T** at 40 °C in CH_2Cl_2 (Run 1)



dimer *T* dimer *D*

Lewis acid-promoted AHDA reaction

Very little is known about the Lewis acid-promoted HDA reaction with a thiabutadiene and a thia-dienophile system.[2–8,10,11] The main reason might be that such thiocarbonyl compounds are generally labile and susceptible to polymerization and decomposition in the presence of an acid and therefore it requires a controlled technique for their generation and effective trapping. In a previous paper we disclosed for the first time that Lewis acids could be used for catalysing the HDA reaction of thiochalcones **1** with a variety of achiral, carbonyl-activated dienophiles.[13] In the present study we have extended the procedure to this AHDA reaction. The results are summarized in Table 2. Characteristic features are as follows: (1) stoichiometrically suitable amounts of a Lewis acid in an appropriate solvent were needed to accelerate significantly the reaction at 25–35 °C and to give fair yields of the cycloadducts as compared with the uncatalysed one at 35–40 °C; (2) almost no change in *endo*-selectivity (*endo vs. exo*) was observed as compared with the thermal reaction; (3) the dimer **D** (for substrate **1a**) gave relatively better chemical yields of the cycloadducts than did the dimers T (for substrates **1d,e,f**); (4) the best π-facial des were attained when the reactions were performed under the following conditions; $AlCl_3$ (3.0 mol

† *endo* refers to a *cis*-relationship between the substituents at the 3- and 4-position of the dihydrothiopyran ring formed, and *exo* to a *trans*-relationship.

‡ For convenience we employed dimers **T** instead of dimers **D** for the reactions of compounds **1d–f** because of inaccessibility of the latter of **1d–f**.

Table 2 Lewis acid-promoted asymmetric hetero-Diels–Alder reaction of thiabutadienes **1** with di-(−)-menthyl fumarate **2**

Run[a]	Thioketone[b]	Lewis acid (mol equiv.)	Solvent	Temperature (T/°C)	Time (t/h)	Cycloadduct	Yield (%)[c]	Ratio of *endo* isomers **3**:**4** (% de)[d,e]
1	**1a**	None	Et_2O	35	36	**3a–6a**	94	59.5:40.5 (19)
2	**1a**	$AlCl_3$ (1.0)	Et_2O	35	7	**3a–6a**	78	79.5:20.5 (59)
3	**1a**	$AlCl_3$ (2.0)	Et_2O	35	5	**3a–6a**	73	77:23 (64)
4	**1a**	$AlCl_3$ (3.0)	Et_2O	35	5	**3a–6a**	76	85.5:14.5 (71)
5	**1a**	$AlCl_3$ (4.0)	Et_2O	35	4	**3a–6a**	55	82:18 (64)
6	**1a**	$EtAlCl_2$ (3.0)	Et_2O	35	8	**3a–6a**	79	77:23 (54)
7	**1a**	$EtAlCl_2$ (4.0)	Et_2O	35	7	**3a–6a**	87	78:22 (56)
8	**1a**	$EtAlCl_2$ (2.0)	CH_2Cl_2	25	0.2	**3a–6a**	84	84:16 (68)
9	**1a**	Pr^iOAlCl_2 (4.0)	Et_2O	35	5	**3a–6a**	89	77:23 (54)
10	**1a**	BF_3 (4.0)	Et_2O	35	18	**3a–6a**	75	59.5:40.5 (19)
11	**1a**	$ZnCl_2$ (4.0)	Et_2O	35	20	**3a–6a**	95	64:36 (28)
12	**1a**	$SnCl_2$ (4.0)	Et_2O	35	10	**3a–6a**	36	67:33 (34)
13	**1d**	$AlCl_3$ (1.0)	Et_2O	25	32	**3d–6d**	28	74.5:25.5 (49)
14	**1d**	Me_2AlCl (1.0)	CH_2Cl_2	25	24	**3d–6d**	87	83:17 (66)
15	**1d**	$EtAlCl_2$ (0.5)	CH_2Cl_2	25	46	**3d–6d**	62	80.5:19.5 (61)
16	**1d**	$EtAlCl_2$ (1.0)	CH_2Cl_2	25	22	**3d–6d**	64	81.5:18.5 (63)
17	**1d**	$EtAlCl_2$ (2.0)	CH_2Cl_2	25	22	**3d–6d**	87	85.5:14.5 (71)
18	**1e**	Me_2AlCl (1.0)	CH_2Cl_2	25	24	**3e–6e**	31	62.5:37.5 (25)
19	**1e**	$EtAlCl_2$ (0.5)	CH_2Cl_2	25	27	**3e–6e**	29	62.5:37.5 (25)
20	**1e**	$EtAlCl_2$ (1.0)	CH_2Cl_2	25	24	**3e–6e**	34	78.5:11.5 (57)
21	**1e**	$EtAlCl_2$ (2.0)	CH_2Cl_2	25	21	**3e–6e**	52	85:15 (70)
22	**1f**	Me_2AlCl (1.0)	CH_2Cl_2	25	9	**3f–6f**	40	62:38 (24)
23	**1f**	$EtAlCl_2$ (0.5)	CH_2Cl_2	25	4	**3f–6f**	38	77.5:22.5 (55)
24	**1f**	$EtAlCl_2$ (1.0)	CH_2Cl_2	25	3	**3f–6f**	47	77:23 (55)
25	**1f**	$EtAlCl_2$ (2.0)	CH_2Cl_2	25	3	**3f–6f**	47	81:19 (62)

[a] The reactions were carried out in molar proportions of **1**:**2**:L.A. = 1:1.2–4.2:0.5–4.0. [b] A dithiine-type dimer **D** was used for **1a** and thiopyran-type dimers **T** for **1d–f**.‡ [c] Isolated total yield of diastereoisomers. [d] Ratios of *endo* (**3** + **4**):*exo* (**5** + **6**) isomers were observed 96:4 ± 1 for **1a**, 97:3 ± 1 for **1d**, 95:5 ± 2 for **1e** and 94:6 ± 1 for **1f**. [e] Determined by HPLC analysis and ^1H NMR (270 or 500 MHz) spectroscopy. ‡ See footnote in text.

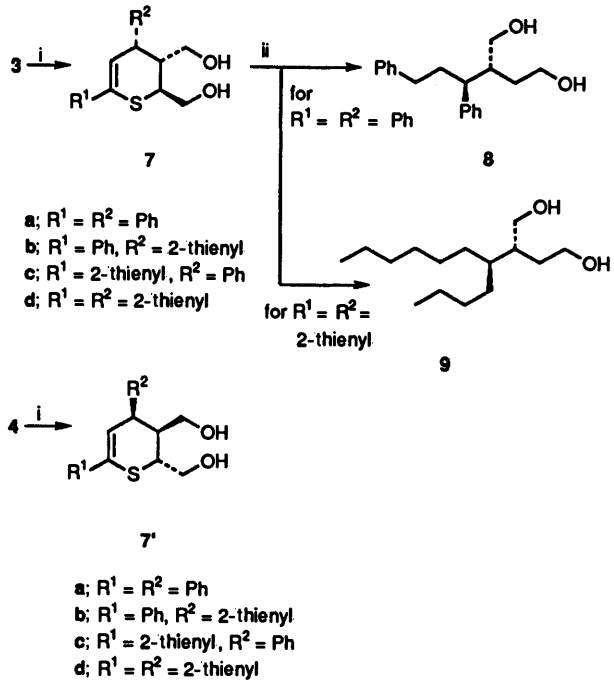
equiv.) in Et_2O, or $EtAlCl_2$ (2.0 mol equiv.) in CH_2Cl_2 (Runs 4, 8, 17, 21 and 25).

Conversion of the cycloadducts 3 into the optically pure diols 7 and 8

Although the π-facial des attained in both thermal and Lewis acid-promoted reactions were not high enough, the major isomer **3** could easily be obtained diastereochemically homogeneous by chromatographic separation of the 3,4-*cis*-adducts **3** and **4** from the 3,4-*trans*-adducts **5** and **6**, followed by several recrystallizations of the former mixture. Each isomer **4**–**6** could also be separated stereochemically pure in certain cases by preparative TLC and repetitive recrystallization. Compound **3** thus obtained was reduced with $LiAlH_4$ to the optically pure diol **7**, which was then further converted into the acyclic diol **8** or **9** by reductive desulfurization with Raney Ni. As expected, the minor 3,4-*cis*-adduct **4** also afforded, by removal of the chiral auxiliary with $LiAlH_4$-reduction, the antipode diol **7′**, whose ^1H NMR spectrum was consistent with that of isomer **7**, confirming them to be enantiomers.

Stereochemical assignments

The structural, relative configurational and conformational assignments were based on ^1H NMR spectroscopy (270 or 500 MHz). For the 3,4-*cis*-adducts **3** and **4** the coupling constants $J_{2,3}$ between H-2 and H-3 protons and $J_{3,4}$ between H-3 and H-4 protons were observed in the ranges 11.1–12.2 Hz and 4.3–4.8 Hz, respectively, the former being consistent with their *trans*-diaxial arrangements and the latter with a *gauche* relationship. Accordingly, the thiopyran ring takes a half-chair conformation in which both (−)-menthoxycarbonyl groups occupy equatorial positions and the R^2 group an axial one. These configurational and conformational stereochemistries deduced by ^1H NMR spectroscopy in solution were in full agreement with those in the crystalline state solved by X-ray analysis. On the other hand, the 3,4-*trans*-adducts **5** and **6** adopt a half-chair conformation about the thiopyran ring with the 2-, 3- and 4-substituent all in



Scheme 2 *Reagents and conditions:* i, $LiAlH_4$, Et_2O or THF, 0 °C; ii, Raney Ni (W-2), EtOH or THF, room temp.

equatorial arrangements, as deduced from the coupling constants $J_{2,3}$ 10.6–11.7 Hz and $J_{3,4}$ 10.6–10.7 Hz of the protons in *trans*-diaxial relationships.[13]

In our preliminary paper the predominant isomer of the *cis*-cycloadducts which had been formed favourably in both thermal and Lewis acid-promoted reactions had the same configuration which was tentatively assigned as 2*R*,3*S*,4*S* (**4**) on the basis of the simple Prelog-model consideration that the

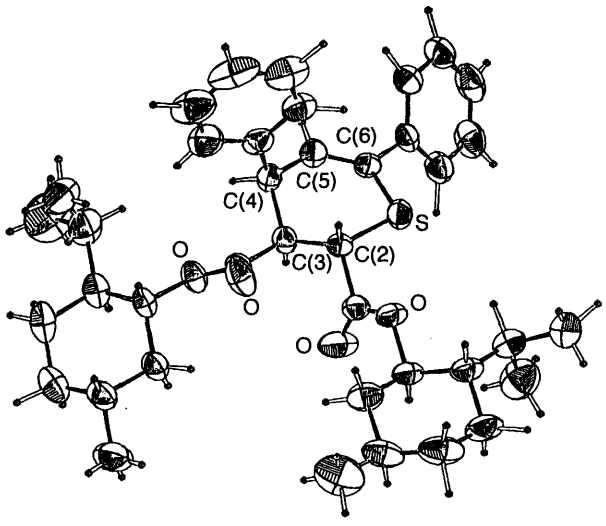


Fig. 2 A molecular structure of compound **3a**

heterodiene **1** would preferentially attack the less hindered *re-re* face of the dienophile **2**.[10] However, the X-ray crystallographic analysis (Fig. 2) confirmed that the configuration of the predominant isomer is 2*S*,3*R*,4*R* (**3**), suggesting that the cycloaddition occurred preferably from the *si-si* face of diester **2**. The sense of this cycloaddition face-selectivity is in conformity with that observed by Walborsky *et al.* in the Lewis acid-catalysed ADA reaction of diester **2** with butadienes.[14] Noteworthy is the temperature effect on the selectivity in the thermal reaction. In our cases, the selectivity is the same as in both the thermal and Lewis acid-promoted reactions (as far as reactions at 20–40 °C are concerned), while in their cases the selectivity for the thermal reaction at a temperature between 180 and 26 °C showed the opposite, though the de values are quite small (0–3%), trend to that for the catalysed one. This small but significant difference between the two reactions of the same dienophile **2** with the different dienes would arise as a consequence of a conformationally temperature-sensitive structure in either transition state that consists of both a diene and a dienophile.

In conclusion, the AHDA reaction between readily available thiochalcones and di-(−)-menthyl furnarate has been shown to give the cycloadducts in excellent yield with fairly good stereoselectivity, and that its application provides a useful method for the synthesis of optically active organic compounds.

Experimental

Mps were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded on a Hitachi Model 270-30 spectrometer. ^{1}H and ^{13}C NMR spectra were measured on JEOL JNM-EX 270 (270 MHz, 67.8 MHz) and/or JEOL JNM-GSX 500 (500 MHz; 125 MHz) spectrometers for solutions in deuteriochloroform, using tetramethylsilane as internal standard. *J* Values are given in Hz. Mass spectra were obtained with a Hitachi Model RMU-7M double-focusing mass spectrometer at an ionizing potential of 70 eV and/or with a Hitachi Model M-80 spectrometer with a data processing system M-003. Optical rotations were measured with a JASCO DIP-370 digital polarimeter and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed on a Yanaco MT-3 CHN recorder. Analytical high-performance liquid chromatography (HPLC) employed JASCO-LABOC and/or Millipore Waters TM-996 instruments using Shiseido Capcell Pak C18 SG120 (4.6 × 250 mm) and DiaChroma Column Silica N (4.6 × 250 mm) eluted with acetonitrile, methanol–water or hexane–ethyl acetate. Column chromatography and preparative (PLC) and analytical TLC were performed on silica gel, Wakogel C-200 and B-5F and Merck Kieselgel 60 F_{254} plates, respectively. Solvents were purified by the usual method before use. Reactions were carried out under argon.

Thermal reaction of the thiabutadiene 1 with the dienophile 2. General procedure

A solution of a mixture of dimer **D** or T of a thiochalcone **1** (1.5 mmol as monomer) and the diester **2** (1.8 mmol, 709 mg) in an appropriate solvent (45 cm^3) (Table 1) was stirred at 40 °C until the dimer disappeared. The solvent was removed by evaporation under reduced pressure and the residue was subjected to column chromatography on silica gel, using hexane–benzene (9:1–1:1) as eluent to give a mixture of cycloadducts **3**–**6** as crystals or an oil. Ratios of the isomers were determined by ^{1}H NMR spectroscopy (5-H proton as the integral marker) and/or analytical HPLC measurements which were performed after and before the column chromatography. The *endo* major isomer **3** was obtained pure by several recrystallizations from ethyl acetate–ethanol. In some cases the other isomers **4** and **5** could be separated in pure forms from the mother liquor by PLC [silica gel; hexane–ethyl acetate (30–40:1)].

Lewis acid-promoted reaction of a thiabutadiene 1 with the dienophile 2. General procedure

Aluminium chloride (1.0–4.0 mol equiv.) was added to dry, stirred diethyl ether (2 cm^3) at 35 or 25 °C under argon. To the resultant solution was added the diester **2** (1.2–4.2 mol equiv.), and then compound **1**-dimer (0.2 mmol as a monomer) was added at the same temperature. For the other Lewis acids, a Lewis acid was added to a solution of the diester **2** in dichloromethane (6 cm^3) or diethyl ether (6 cm^3) and then compound **1**-dimer was added to the solution. After completion of the reaction, the reaction was quenched with saturated aq. ammonium chloride and the reaction mixture was extracted with diethyl ether. The organic layer was washed successively with saturated aq. sodium hydrogen carbonate and saturated aq. sodium chloride and then dried ($MgSO_4$). Procedures for the analysis, isolation and purification of the cycloadducts were the same as above.

Di-(−)-menthyl (2*S*,3*R*,4*R*)-4,6-diphenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 3a (*endo* major). Needles, mp 128.7–129.7 °C (Found: C, 75.6; H, 8.8. $C_{39}H_{52}O_4S$ requires C, 75.9; H, 8.5%); $[\alpha]_D$ +237 (*c* 2.0, benzene); HPLC (t_R 21.76 min; MeCN 1 cm^3 min^{-1}); *m*/*z* 616 (M^+, 0.4%), 477 (M^+ − menthyl, 29), 339 (M^+ − 2 menthyl, 65), 321 (32), 223 (53) and 83 (100); ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.60–7.00 (m, 10 H, ArH), 6.20 (d, 1 H, *J* 6.7, 5-H), 4.85–4.35 (m, 2 H, OCH), 4.23 (d, 1 H, *J* 11.1, 2-H), 4.16 (dd, 1 H, *J* 6.7 and 4.5, 4-H), 3.39 (dd, 1 H, *J* 11.1 and 4.5, 3-H) and 2.28–0.40 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 171.41 (s), 170.19 (s), 139.63 (s), 138.85 (s), 133.59 (s, C-6), 129.93 (d × 2), 128.62 (d × 3), 128.52 (d × 2), 127.59 (d), 126.76 (d × 2), 120.72 (d, C-5), 76.03 (d), 75.54 (d), 47.08 (d × 2), 46.01 (d, C-2), 42.69 (d, C-4), 40.69 (d, t, C-3), 40.31 (t), 34.26 (t × 2), 31.43 (d × 2), 25.88 (d), 25.68 (d), 23.15 (t), 22.81 (t), 22.08 (q × 2) 21.25 (q), 20.96 (q), 16.04 (q) and 15.79 (q).

Di-(−)-menthyl (2*R*,3*S*,4*S*)-4,6-diphenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 4a (*endo* minor). HPLC (t_R 21.76 min; MeCN 1 cm^3 min^{-1}); ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.58–7.02 (m, 10 H, ArH), 6.19 (d, 1 H, *J* 6.8, 5-H), 4.89–4.37 (m, 2 H, OCH), 4.25 (d, 1 H, *J* 12.2, 2-H), 4.20 (dd, 1 H, *J* 6.8 and 4.8, 4-H), 3.40 (dd, 1 H, *J* 12.2 and 4.8, 3-H) and 2.16–0.52 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 170.90 (s), 169.90 (s), 139.63 (s), 138.85 (s), 133.59 (s), 129.93 (d × 2), 128.62 (d × 3), 128.52 (d × 2), 127.59 (d), 126.76 (d × 2), 120.72 (d, C-5), 76.03 (d), 75.54 (d), 47.08 (d × 2), 46.01 (d, C-2), 42.69 (d, C-4), 40.69 (d, t, C-3) 40.31 (t), 34.26 (t × 2), 31.43 (d × 2), 25.88 (d), 25.68 (d), 23.15 (t), 22.81 (t), 22.08 (q × 2), 21.25 (q), 20.96 (q), 16.04 (q) and 15.79 (q).

Di-(−)-menthyl (2*S*,3*R*,4*R*)-6-phenyl-4-(*p*-tolyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 3b (*endo* major). Needles, mp 185.5–186.8 °C (Found: C, 76.1; H, 8.75, $C_{40}H_{54}O_4S$ requires C, 76.15; H, 8.6%); $[\alpha]_D$ +228 (*c* 2.0, benzene); *m*/*z* 630 (M^+, 1%), 491 (M^+ − menthyl, 56), 353 (M^+ − 2 menthyl + 1, 76), 335 (21), 263 (26), 238 (thione$^+$, 10), 139 (menthyl$^+$, 16) and 83 (100); ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.52–7.08 (m, 9 H, ArH), 6.21 (d, 1 H, *J* 6.6, 5-H), 4.74–4.65 (m, 1 H, OCH), 4.58–4.51 (m, 1 H, OCH), 4.23 (d, 1 H, *J* 11.4, 2-H), 4.14 (dd, 1 H, *J* 6.6 and 4.8, 4-H), 3.38 (dd, 1 H, *J* 11.4 and 4.8, 3-H), 2.31 (s, 3 H, Me) and 2.05–0.54 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 171.41 (s), 170.09 (s), 138.85 (s), 137.10 (s), 136.47 (s), 133.25 (s, C-6), 129.11 (d × 2), 128.47 (d × 3), 126.62 (d × 2), 120.77 (d, C-5), 75.88 (d), 75.35 (d), 46.98 (d × 2), 46.09 (d, C-2), 42.30 (d, C-4), 40.55 (d, t, C-3), 40.21 (t), 34.21 (t × 2), 31.34 (d × 2), 25.83 (d), 25.29 (d), 23.10 (t), 22.71 (t), 21.98 (q × 2), 21.15 (q), 20.86 (q), 15.94 (q) and 15.74 (q).

Di-(−)-menthyl (2*R*,3*S*,4*S*)-6-phenyl-4-(*p*-tolyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 4b (*endo* minor). *m*/*z* 630 (M^+, 0.3%), 491 (M^+ − menthyl, 22), 353 (M^+ − 2menthyl + 1, 30), 335 (10), 63 (12), 238 (thione$^+$, 6), 139 (menthyl$^+$, 12) and 83 (100); ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.52–7.08 (m, 9 H, ArH), 6.20 (d, 1 H, *J* 7.7, 5-H), 4.74–4.65 (m, 1 H, OCH), 4.58–4.51 (m, 1 H, OCH), 4.26 (d, 1 H, *J* 11.7, 2-H), 4.18 (dd, 1 H, *J* 7.7 and 4.4, 4-H), 3.39 (dd, 1 H, *J* 11.7 and 4.4, 3-H), 2.30 (s, 3 H, Me) and 2.05–0.54 (m, 36 H, menthyl).

Di-(−)-menthyl (2*S*,3*R*,4*R*)-4-(*p*-chlorophenyl)-6-phenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 3c (*endo* major). *m*/*z* 650 (M^+, 0.3%), 511 (M^+ − menthyl, 24), 373 (M^+ − 2 menthyl + 1, 35), 139 (menthyl$^+$, 27) and 83 (100); ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.52–7.13 (m, 9 H, ArH), 6.183 (d, 1 H, *J* 6.6, 5-H), 4.73–4.66 (m, 1 H, OCH), 4.59–4.48 (m, 1 H, OCH), 4.18 (d, 1 H, *J* 11.4, 2-H), 4.16 (dd, 1 H, *J* 6.6 and 4.8, 4-H), 3.40 (dd, 1 H, *J* 11.4 and 4.8, 3-H) and 2.07–0.55 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 171.17 (s), 169.95 (s), 138.61 (s), 138.12 (s), 134.08 (s), 133.49 (s, C-6), 130.52 (d × 2), 128.62 (d × 4), 126.67 (d × 3), 120.04 (d, C-5), 76.13 (d), 75.59 (d), 46.76 (d × 2, C-2), 45.76 (d × 2), 42.01 (d, C-4), 40.55 (dt, C-3), 40.31 (t), 34.21 (t × 2), 31.44 (d × 2), 25.83 (d), 23.10 (t), 22.76 (t), 21.98 (q × 2), 21.15 (q), 20.91 (q), 15.94 (q) and 15.74 (q).

Di-(−)-menthyl (2*R*,3*S*,4*S*)-4-(*p*-chlorophenyl)-6-phenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 4c (*endo* minor). ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.52–7.13 (m, 9 H, ArH), 6.175 (d, 1 H, *J* 7.0, 5-H), 4.73–4.66 (m, 1 H, OCH), 4.59–4.48 (m, 1 H, OCH), 4.20 (d, 1 H, *J* 11.7, 2-H), 4.20 (dd, 1 H, *J* 7.0 and 4.4, 4-H), 3.40 (dd, 1 H, *J* 11.7 and 4.4, 3-H) and 2.07–0.55 (m, 36 H, menthyl).

Di-(−)-menthyl (2*S*,3*R*,4*S*)-4-(*p*-chlorophenyl)-6-phenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 5c (*exo* major). ν_{max}(KBr)/cm^{-1} 1720 (C=O); δ_H($CDCl_3$) 7.47–7.18 (m, 9 H, ArH), 5.96 (d, 1 H, *J* 2.5, 5-H), 4.74–4.69 (m, 1 H, OCH), 4.69–4.38 (m, 1 H, OCH), 4.49 (d, 1 H, *J* 10.6, 2-H), 3.75 (dd, 1 H, *J* 10.6 and 2.5, 4-H), 3.19 (d, 1 H, *J* 10.6, 3-H) and 2.06–0.66 (m, 36 H, menthyl).

Di-(−)-menthyl (2*R*,3*S*,4*R*)-4-(*p*-chlorophenyl)-6-phenyl-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate (6c, *exo* minor). ν_{max}(KBr)/cm^{-1} 1720 (C=O); δ_H($CDCl_3$) 7.47–7.18 (m, 9 H, ArH), 5.86 (d, 1 H, *J* 2.9, 5-H), 4.74–4.69 (m, 1 H, OCH), 4.69–4.38 (m, 1 H, OCH), 4.52 (d, 1 H, *J* 11.7, 2-H), 3.82 (dd, 1 H, *J* 11.7 and 2.9, 4-H), 3.20 (d, 1 H, *J* 11.7, 3-H) and 2.06–0.66 (m, 36 H, menthyl).

Di-(−)-menthyl (2*S*,3*R*,4*R*)-6-phenyl-4-(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 3d (*endo* major). Cubes, mp 150.5–151.0 °C (Found: C, 71.2; H, 8.3, $C_{37}H_{50}O_4S_2$ requires C, 71.35: H, 8.1%); *m*/*z* 622 (M^+, 10%), 483 (M^+ − menthyl, 50), 345 (M^+ − 2 menthyl, 50), 139 (menthyl$^+$, 15) and 83 (100); ν_{max}(KBr)/cm^{-1} 1732 (C=O); δ_H($CDCl_3$) 7.50–6.85 (m, 8 H, ArH), 6.26 (d, 1 H, *J* 5.4 and 6.60, 5-H), 4.70 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.63 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.48 (dd, 1 H, $J_{4,3}$ 4.29 and $J_{4,5}$ 6.60, 4-H), 4.32 (d, 1 H, $J_{2,3}$ 11.22, 2-H), 3.40 (dd, 1 H, $J_{3,4}$ 4.29 and $J_{3,2}$ 11.22, 3-H) and 2.07–0.68 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 171.16 (s), 170.11 (s), 142.30 (s), 133.60 (s), 133.48 (s), 128.66 (d), 128.55 (d), 128.34 (d), 126.90 (d), 126.77 (d × 2), 126.36 (d), 125.28 (d), 120.59 (d), 75.99 (d), 75.63 (d), 47.01 (d × 2), 46.97 (d), 46.09 (d), 40.81 (d), 40.57 (t), 40.31 (t), 37.74 (d), 34.20 (t), 31.41 (t), 31.37 (d), 25.79 (d), 25.46 (d), 23.04 (t), 22.79 (t), 22.05 (q), 21.99 (q), 21.17 (q), 20.88 (q) and 15.92 (q × 2).

Di-(−)-menthyl (2*R*,3*S*,4*S*)-6-phenyl-4-(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 4d (*endo* minor). Cubes, mp 150–151 °C; *m*/*z* 622 (M^+, 10%) and 83 (thienyl$^+$, 100); ν_{max}(KBr)/cm^{-1} 1732 (C=O); δ_H($CDCl_3$) 7.50–6.88 (m, 8 H, ArH), 6.24 (d, 1 H, $J_{5,4}$ 6.60, 5-H), 4.73 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.63 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.51 (dd, 1 H, $J_{4,3}$ 4.29 and $J_{4,5}$ 6.60, 4-H), 4.32 (d, 1 H, $J_{2,3}$ 11.22, 2-H), 3.38 (dd, 1 H, $J_{3,4}$ 4.29 and $J_{3,2}$ 11.22, 3-H) and 2.06–0.61 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 170.74 (s), 169.81 (s), 142.17 (s), 138.52 (s), 133.33 (s), 128.66 (d), 128.55 (d × 2), 126.97 (d), 126.77 (d × 2), 126.467 (d), 125.28 (d), 120.63 (d), 75.56 (d), 75.46 (d), 46.88 (d), 46.72 (d), 45.55 (d), 40.52 (t), 40.40 (t), 40.32 (d), 37.77 (d), 34.16 (t), 31.11 (t), 31.37 (d × 2), 25.75 (d), 25.55 (d), 23.20 (t), 22.05 (t), 21.99 (q), 21.04 (q), 20.92 (q), 20.81 (q) and 16.33 (q × 2).

Di-(−)-menthyl (2*S*,3*R*,4*S*)-6-phenyl-4-(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 5d (*exo* major). δ_H($CDCl_3$) 7.32–6.96 (m, 8 H, ArH), 6.07 (d, 1 H, $J_{5,4}$ 2.97, 5-H), 4.76–4.67 (m, 2 H, OCH × 2), 4.49 (d, 1 H, $J_{2,3}$ 10.88, 2-H), 3.79 (dd, 1 H, $J_{4,5}$ 2.97, $J_{4,3}$ 10.88, 4-H), 3.32 (t, 1 H, $J_{3,4}$ = $J_{3,2}$ = 10.88, 3-H) and 2.00–0.54 (m, 36 H, menthyl).

Di-(−)-menthyl (2*S*,3*R*,4*R*)-4-phenyl-6-(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 3e (*endo* major). Crystals; mp 131.6–132.5 °C (Found: C, 71.3; H, 8.1 $C_{37}H_{50}O_4S_2$ requires C, 71.35; H, 8.1%); *m*/*z* 622 (M^+, 5%), 483 (M^+ − menthyl, 38), 345 (M^+ − 2 menthyl, 47), 139 (menthyl$^+$, 23) and 83 (thienyl$^+$, 100); ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.35–6.95 (m, 8 H, ArH), 6.35 (d, 1 H, $J_{5,4}$ 6.60, 5-H), 4.68 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.54 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.26 (d, 1 H, $J_{2,3}$ 11.22, 2-H), 4.16 (dd, 1 H, $J_{4,3}$ 4.62 and $J_{4,5}$ 6.60, 4-H), 3.40 (dd, 1 H, $J_{3,4}$ 4.62 and $J_{3,2}$ 11.22, 3-H) and 1.69–0.53 (m, 36 H, menthyl); δ_C($CDCl_3$, DEPT) 171.12 (s), 169.81 (s), 141.29 (s), 139.23 (s), 129.22 (d × 2), 128.46 (d), 127.62 (d), 127.33 (d × 2), 126.75 (s), 124.83 (d), 124.24 (d), 120.07 (d), 76.10 (d), 75.52 (d), 47.01 (d), 46.90 (d), 46.04 (d), 42.48 (d), 40.72 (d), 40.57 (t), 40.16 (t), 34.17 (t), 34.12 (t), 31.39 (d), 31.32 (d), 25.82 (d), 25.55 (d), 23.04 (t), 22.68 (t), 21.98 (q × 2), 21.13 (q), 20.90 (q), 15.92 (q) and 15.69 (q).

Di-(−)-menthyl (2*R*,3*S*,4*S*)-4-phenyl-6-(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 4e (*endo* minor). ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$) 7.23–6.98 (m, 8 H, ArH), 6.34 (d, 1 H, $J_{5,4}$ 6.60, 5-H), 4.72 (ddd, 1 H, *J* 4.62, 10.89 and 10.89, OCH), 4.52 (ddd, 1 H, *J* 4.62, 10.89 and 10.89, OCH), 4.27 (d, 1 H, $J_{2,3}$ 11.22, 2-H), 4.19 (dd, 1 H, $J_{4,3}$ 4.62 and $J_{4,5}$ 6.60, 4-H), 3.38 (dd, 1 H, $J_{3,4}$ 4.62 and $J_{3,2}$ 11.22, 3-H) and 2.00–0.54 (m, 36 H, menthyl); δ_C($CDCl_3$; DEPT) 170.67 (s), 169.61 (s), 141.22 (s), 139.26 (s), 129.25 (d × 2), 128.57 (d × 2), 127.73 (d), 127.33 (d), 126.65 (s), 124.83 (d), 124.38 (d), 120.34 (d), 75.69 (d), 75.42 (d), 46.74 (d × 2), 45.48 (d), 42.55 (d), 40.56 (t), 40.41 (t), 40.22 (d), 34.16 (t), 34.09 (t), 31.39 (d), 31.32 (d), 25.71 (d), 25.53 (d), 23.18 (t), 22.01 (q × 2), 20.83 (q × 2), 16.42 (q) and 16.28 (q).

Di-(−)-menthyl (2*S*,3*R*,4*S*)-4-phenyl-6-(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 5e (*exo* major). ν_{max}(KBr)/cm^{-1} 1734 (C=O); δ_H($CDCl_3$); 7.35–6.95 (m, 8 H, ArH), 6.06 (d, 1 H, $J_{5,4}$ 2.97, 5-H), 4.73–4.67 (m, 2 H, OCH × 2), 4.47 (d, 1 H, $J_{2,3}$ 10.89, 2-H), 3.76 (dd, 1 H, $J_{4,5}$ 2.97 and $J_{4,3}$ 10.89, 4-H), 3.25 (t, 1 H, $J_{3,4}$ = $J_{3,2}$ = 10.89, 3-H) and 1.69–0.53 (m, 36 H, menthyl).

Di-(−)-menthyl (2*S*,3*R*,4*R*)-4,6-di(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 3f (*endo* major). Crystals, mp

109.2–111.0 °C (Found: C, 66.7; H, 7.7. $C_{35}H_{48}O_4S_3$ requires C, 66.8; H, 7.7%); $[\alpha]_D$ +159.7 (*c* 1.93, $CHCl_3$); *m/z* 628 (M^+, 10%), 489 (M^+ − menthyl, 45), 351 (M^+ − 2 menthyl, 40), 138 (menthyl$^+$, 20) and 83 (thienyl$^+$, 100); ν_{max}(KBr)/cm^{-1} 1732 (C=O). δ_H($CDCl_3$) 7.26–6.84 (m, 6 H, ArH), 6.39 (d, 1 H, $J_{5,4}$ 6.60, 5-H), 4.70 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.62 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.46 (dd, 1 H, $J_{4,3}$ 4.29 and $J_{4,5}$ 6.60, 4-H), 4.34 (d, 1 H, $J_{2,3}$ 11.22, 2-H), 3.38 (dd, 1 H, $J_{3,4}$ 4.29 and $J_{3,2}$ 11.22, 3-H) and 2.07–0.77 (m, 36 H, menthyl); δ_C($CDCl_3$, DEPT) 170.87 (s), 169.79 (s), 141.87 (s), 140.99 (s), 127.37 (d), 126.86 (d), 126.72 (d), 126.52 (d), 125.35 (d), 125.05 (d), 124.51 (d), 119.91 (d), 76.10 (d), 75.67 (d), 58.47 (t), 46.95 (d × 2), 46.24 (d), 40.90 (d), 40.54 (t), 40.23 (t), 37.65 (d), 34.16 (t), 31.39 (d), 31.34 (d), 25.80 (d), 25.43 (d), 23.00 (t), 22.73 (t), 22.01 (q), 21.98 (q), 21.15 (q), 20.88 (q) and 15.90 (q × 2).

Di-(−)-menthyl (2*R*,3*S*,4*S*)-4,6-di(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 4f (*endo* minor). δ_H($CDCl_3$) 7.23–6.87 (m, 6 H, ArH), 6.38 (d, 1 H, $J_{5,4}$ 6.60, 5-H), 4.73 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.62 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.49 (dd, 1 H, $J_{4,3}$ 4.29 and $J_{4,5}$ 6.60, 4-H), 4.33 (d, 1 H, $J_{2,3}$ 11.22, 2-H), 3.77 (dd, 1 H, $J_{3,4}$ 4.29 and $J_{3,2}$ 11.22, 3-H) and 2.05–0.61 (m, 36 H, menthyl); δ_C($CDCl_3$) 170.49 (s), 169.52 (s), 141.74 (s), 140.91 (s), 127.35 (d), 126.97 (d), 126.66 (s), 126.61 (d), 125.39 (d), 125.05 (d), 124.62 (d), 120.05 (d), 75.69 (d), 75.49 (d), 60.39 (t), 46.86 (d), 46.72 (d), 45.73 (d), 40.52 (t), 40.45 (d), 40.38 (t), 37.66 (d), 34.14 (t), 31.37 (d), 25.75 (d), 25.57 (d), 23.18 (t × 2), 22.01 (d), 20.90 (q × 2), 20.81 (q), 16.33 (q × 2) and 14.20 (q).

Di-(−)-menthyl (2*S*,3*R*,4*S*)-4,6-di(2-thienyl)-3,4-dihydro-2*H*-thiopyran-2,3-dicarboxylate 5f (*exo* major). δ_H($CDCl_3$) 7.26–6.90 (m, 6 H, ArH), 6.11 (d, 1 H, $J_{5,4}$ 2.97, 5-H), 4.71 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.50 (ddd, 1 H, *J* 4.29, 10.89 and 10.89, OCH), 4.46 (d, 1 H, $J_{2,3}$ 10.89, 2-H), 4.18 (dd, 1 H, $J_{4,5}$ 2.97 and $J_{4,3}$ 10.89, 4-H), 3.25 (t, 1 H, $J_{3,4}$ = $J_{3,2}$ 10.89, 3-H) and 1.99–0.67 (m, 36 H, menthyl).

Reduction of the diesters 3 and 4 with $LiAlH_4$ to give the diols 7 and 7′. (2*S*,3*R*,4*R*)-2,3-Bis(hydroxymethyl)-4,6-diphenyl-3,4-dihydro-2*H*-thiopyran 7a

To a suspension of $LiAlH_4$ (95 mg, 2.5 mmol) in diethyl ether (50 cm^3) was added an ethereal solution (20 cm^3) of the diester **3a** (308 mg, 0.50 mmol) at 0 °C. The reaction mixture was stirred for 3 h at the same temperature, quenched successively with water (0.5 cm^3) and saturated aq. NH_4Cl, and dried (Na_2SO_4). Filtration through Celite, evaporation off of the solvent, chromatography of the residue [silica gel (80 cm^3); hexane–ethyl acetate (4:1)] and recrystallization of the major product from hexane–ethyl acetate gave the *diol* **7a** (137 mg, 88%) as needles, mp 205–206 °C (Found: C, 72.95; H, 6.7. $C_{19}H_{20}O_2S$ requires C, 73.0; H, 6.45%); $[\alpha]_D$ +24.4 (*c* 1.0, EtOH); *m/z* 312 (M^+, 12%), 294 (M^+ − H_2O, 7), 276 (M^+ − $2H_2O$, 16), 236 (M^+ − $SCHCH_2OH$, 41) and 223 [M^+ − 2 ($CHCH_2OH$) − H, 100]; ν_{max}(KBr)/cm^{-1} 3256 (OH), 1028 and 1016; δ_H($CDCl_3$) 7.64–7.00 (m, 10 H, ArH), 6.11 (d, 1 H, *J* 4.0, 5-H), 4.00–3.64 (m, 3 H), 3.64–3.28 (m, 3 H), 3.20–2.76 (m, 1 H) and 2.24–1.84 (m, 2 H); δ_C($CDCl_3$) 141.63 (s), 139.63 (s), 133.73 (s), 128.62 (d × 2), 128.52 (d × 4), 128.32 (d), 127.06 (d), 126.28 (d × 2), 120.72 (d), 64.43 (t), 62.19 (t), 43.72 (d), 40.89 (d) and 40.06 (d). The enantiomer **7′a** showed a ^{1}H NMR spectrum completely identical with that of compound **7a**.

(2*S*,3*R*,4*R*)-2,3-Bis(hydroxymethyl)-6-phenyl-4-(2-thienyl)-3,4-dihydro-2*H*-thiopyran 7b. To a suspension of $LiAlH_4$ (104 mg, 2.7 mmol) in tetrahydrofuran (THF; 4 cm^3) was added a THF solution (6 cm^3) of the diester **3d** (343 mg, 0.55 mmol) at 0 °C. The reaction mixture was stirred for 3 h at the same temperature, diluted with diethyl ether, treated successively with water (0.5 cm^3) and 15% aq. NaOH (0.1 cm^3), and dried ($MgSO_4$). Filtration through Celite, evaporation off of the solvent, chromatography of the residue [silica gel (80 cm^3); hexane–ethyl acetate (2:1)] and recrystallization of the major product from hexane–ethyl acetate gave the diol **7b** (111 mg, 64%) as needles, mp 130.8–131.9 °C; $[\alpha]_D$ +7.4 (*c* 2.0, EtOH); *m/z* 318 (M^+, 25%), 300 (M^+ − H_2O, 10), 229 [M^+ − ($CHCH_2OH$)$_2$ − H, 100] and 31 (CH_2OH^+, 38); ν_{max}(KBr)/cm^{-1} 3236 (OH); δ_H([$^2H_6$]Me_2SO) 7.68–7.13 (m, 8 H, ArH), 6.33 (d, 1 H, $J_{5,4}$ 4.95, 5-H), 5.30 (t, 1 H, *J* 5.61, OH), 4.81 (t, 1 H, *J* 4.95, OH), 4.38 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 4.95, 4-H), 3.93–3.76 (m, 2 H, CH_2), 3.64–3.53 (m, 2 H, CH_2), 3.27 (dt, 1 H, *J* 5.61 and $J_{2,3}$ 10.89, 2-H) and 2.48 (ddt, 1 H, $J_{3,2}$ 10.89, $J_{3,4}$ 4.95 and *J* 5.61, 3-H); δ_C([$^2H_6$]Me_2SO) 145.18 (s), 139.37 (s), 133.59 (s), 128.63 (d × 2), 128.34 (d), 127.03 (d), 125.93 (d × 2), 125.46 (d), 124.55 (d), 119.88 (d), 63.09 (t), 59.12 (t), 42.91 (d), 40.02 (d) and 34.70 (d). The enantiomer **7′b** showed a ^{1}H NMR spectrum completely identical with that of compound **7b**.

(2*S*,3*R*,4*R*)-2,3-Bis(hydroxymethyl)-4-phenyl-6-(2-thienyl)-3,4-dihydro-2*H*-thiopyran 7c. Similar treatment of the diester **3e** (428 mg, 0.69 mmol) to that of diester **3a** afforded the diol **7c** (131 mg, 60%) as needles, mp 121.5–122.8 °C; $[\alpha]_D$ −0.78 (*c* 2.0, EtOH); *m/z* 318 (M^+, 18%), 300 (M^+ − H_2O, 7), 229 [M^+ − ($CHCH_2OH$)$_2$ − H, 100] and 31 (CH_2OH^+, 32); ν_{max}(KBr)/cm^{-1} 3264 (OH); δ_H([$^2H_6$]Me_2SO) 7.51–7.08 (m, 8 H, ArH), 6.26 (d, 1 H, $J_{5,4}$ 4.95, 5-H), 5.23 (t, 1 H, *J* 5.28, OH), 4.61 (t, 1 H, *J* 4.95, OH), 3.97 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 4.95, 4-H), 3.86–3.70 (m, 2 H, CH_2), 3.57–3.33 (m, 2 H, CH_2), 2.99 (dt, 1 H, *J* 5.28 and 9.90, 2-H) and 2.37 (ddt, 1 H, $J_{3,2}$ 9.90, $J_{3,4}$ 4.95, *J* 5.28, 3-H); δ_C([$^2H_6$]Me_2SO) 142.70 (s), 141.89 (s), 128.68 (d × 2), 128.34 (d × 2), 127.64 (d), 127.10 (s), 126.54 (d), 125.11 (d), 123.33 (d), 119.37 (d), 63.29 (t), 58.69 (t), 43.29 (d), 39.20 (d) and 38.49 (d). The enantiomer **7′c** showed a ^{1}H NMR spectrum completely identical with that of compound **7c**.

(2*S*,3*R*,4*R*)-2,3-Bis(hydroxymethyl)-4,6-di-(2-thienyl)-3,4-dihydro-2*H*-thiopyran 7d. Similar treatment of the diester **3f** (503 mg, 0.80 mmol) to that of diester **3d** afforded the diol **7d** (244 mg, 94%) as needles, mp 91.7–92.4 °C; $[\alpha]_D$ +2.6 (*c* 2.0, EtOH); *m/z* 324 (M^+, 28%), 306 (M^+ − H_2O, 7), 235 [M^+ − ($CHCH_2OH$)$_2$ − H, 100] and 31 (CH_2OH, 32); ν_{max}(KBr)/cm^{-1} 3284 (OH); δ_H([$^2H_6$]Me_2SO) 7.65 (dd, 1 H, *J* 0.66 and 4.62, 2-thienyl), 7.60 (dd, 1 H, *J* 0.66 and 4.62, 2-thienyl), 7.39 (d, 1 H, *J* 3.63, 2-thienyl), 7.22 (dd, 1 H, *J* 3.63 and 4.62, 2-thienyl), 7.20 (dd, 1 H, *J* 3.63 and 4.62, 2-thienyl), 7.12 (d, 1 H, *J* 3.63, 2-thienyl), 6.42 (d, 1 H, $J_{5,4}$ 4.62, 5-H), 5.32 (t, 1 H, *J* 5.61, OH), 4.82 (t, 1 H, *J* 4.62, OH), 4.40 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 4.62, 4-H), 3.94–3.77 (m, 2 H, CH_2), 3.66–3.55 (m, 2 H, CH_2), 3.26 (dt, 1 H, *J* 5.61 and $J_{2,3}$ 10.89, 2-H) and 2.49 (ddt, 1 H, $J_{3,4}$ 4.62, *J* 5.61 and $J_{3,2}$ 10.89, 3-H); δ_C([$^2H_6$]Me_2SO) 144.73 (s), 142.34 (s), 127.69 (d), 127.21 (s), 127.05 (d), 125.59 (d), 125.36 (d), 124.71 (d), 123.58 (d), 119.10 (d), 62.90 (t), 59.14 (t), 43.22 (d), 40.29 (d) and 34.67 (d). The enantiomer **7′d** showed a ^{1}H NMR spectrum identical with that of compound **7d**.

Reductive desulfurization of the diols 7 with Raney Ni to afford the acyclic diol 8 or 9

A mixture of sulfide **7a** or **7d** (1.0 mmol) and Raney Ni (W-2, 5 g) in ethanol or THF (30 cm^3) was stirred overnight at room temperature. The mixture was filtered over Celite and the filtrate was evaporated. The residue was chromatographed over silica gel and eluted with ethyl acetate–hexane (1:8–1:2) to give the acyclic diol **8** (70%) or **9** (47%) each as an oil.

(2*R*,1′*S*)-2-(1,3-Diphenylpropyl)butane-1,4-diol 8. (Found: M^+, 284.1784. $C_{19}H_{24}O_2$ requires *M*, 284.1777); $[\alpha]_D$ +0.58 (*c* 2.0, EtOH); ν_{max}(CCl_4)/cm^{-1} 3356 and 1043; *m/z* 284 (M^+, 1%), 266 (M^+ − H_2O, 6), 220 (5), 117 (34) and 91 (100); δ_H($CDCl_3$) 7.50–6.88 (m, 10 H) and 4.00–0.60 (m, 14 H); δ_C(CCl_4) 143.00 (s), 142.36 (s), 128.52 (d × 2), 128.33 (d × 4), 123.28 (d), 125.69 (d), 63.94 (t), 60.87 (t), 46.50 (d), 44.40 (d), 34.70 (t), 33.92 (t) and 33.24 (d).

(2*R*,1′*S*)-2-(1-Butylheptyl)butane-1,4-diol 9. ν_{max}(neat, NaCl)/cm^{-1} 3340; δ_H($CDCl_3$) 3.80–3.76 (m, 2 H), 3.65–3.45 (m, 4 H), 2.00–1.88 (m, 2 H), 1.85–1.51 (m, 2 H), 1.25 (br s, 16 H) and

0.88 (br s, 6 H); $\delta_C(CCl_4)$ 65.48 (t), 62.28 (t), 42.21 (d), 41.10 (d), 33.58 (t), 31.90 (t), 31.14 (t), 30.78 (t), 30.22 (t), 29.70 (t), 27.92 (t), 23.09 (t), 22.70 (t) and 14.12 (q × 2).

X-Ray crystallographic analysis of compound 3a

Crystal data for compound **3a**. $C_{39}H_{52}O_4S$, $M = 616.87$. Monoclinic, space group $P2_1$, $a = 14.092(4)$, $b = 10.197(1)$, $c = 13.746(4)$ Å, $\beta = 113.21(1)$, $V = 1815.3(8)$ Å^3, $Z = 2$, $D_{calc} = 1.129$ Mg m^{-3}. Crystal dimensions 0.41 × 0.40 × 0.22 mm, μ(Mo-Kα) = 0.119 mm^{-1}, $F(000) = 668$.

Data collection and processing. Enraf-Nonius CAD-4 diffractometer, $\omega/2\theta$ scan mode, ω scan speed ~4 deg min^{-1} (h, −18 to 18; k, 0 to 13; l, 0 to 17; $4° < 2\theta < 55°$), graphite-monochromated Mo-Kα radiation ($\lambda = 0.710\,73$ Å), 3436 reflections measured, 3303 unique reflections with $|F| \geqslant 4\sigma(F)$.

Structure analysis and refinement. The configuration was determined on the basis of the internal standard of the (1*R*,2*S*,5*R*)-(−)-menthoxyl groups. The structure was solved by direct method using MULTAN 78,[15] refined by block-diagonal least-squares with anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms located from difference Fourier maps. Final R-, R_w- and S-values are 0.049, 0.045 and 0.702. The atomic scattering factors and f'-, f''-values were taken from International Tables for X-Ray Crystallography.[16] The refinement was made on a FACOM M1800 computer using UNICS III program,[17] and the illustration in Fig. 2 was produced using the ORTEP program.§[18]

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§ Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/25.

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