Synthesis of bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF) derivatives functionalised with two, four or eight hydroxyl groups

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Short synthetic routes to a range of BEDT-TTF derivatives functionalised with two, four or eight hydroxyl groups are reported, of interest because of their potential for introducing hydrogen bonding between donor and anion into their radical cation salts. The cycloaddition of 1,3-dithiole-2,4,5-trithione with alkenes to construct 5,6-dihydro-1,3-dithiolo[4,5-*b*]1,4-dithiin-2-thiones is a key step, with homo- or hetero-coupling procedures and O-deprotection completing the syntheses. The first synthesis of a single diastereomer of tetrakis(hydroxymethyl)BEDT-TTF, the *cis*,*trans* product, was achieved by careful choice of O-protecting groups to facilitate separation of homo- and hetero-coupled products. Cyclisation of the trithione with enantiopure 1*R*,2*R*,5*R*,6*R*-bis(*O*,*O*-isopropylidene)hex-3-ene-1,2,5,6-tetrol (from D-mannitol) gave two separable diastereomeric thiones, which can be transformed to enantiomeric BEDT-TTF derivatives with four or eight hydroxyl groups.

Introduction

Following on from the extensive studies on tetrathiafulvalene (TTF),[1] bis(ethylenedithio)tetrathiafulvalene, more commonly known as BEDT-TTF or ET **1**, has played a prominent role in the recent development of molecular conductors, superconductors and bifunctional materials, and a wide range of its radical cation salts have been prepared and their properties investigated.[2] Particular highlights are the salts $(ET)_2(Cu(NCS)_2)$ and $(ET)_2(N(CN)_2)X$ (X = Cl or Br) which become superconducting at low temperatures,[3] the paramagnetic superconducting radical salt $(ET)_4[Fe(oxalate)_3]\cdot H_2O\cdot C_6H_5CN$,[4] a layered salt with a mixed chromium(III)/manganese(II) oxalate network which has independent electrical and ferromagnetic properties,[5] and salts with $MHg(SCN)_4^-$ (M = K or Tl) which form a chiral surface metal in a magnetic field.[6] The superconducting salts are of great interest to theoretical physicists since the salts are clean systems whose electrical behaviour can be modelled, and provide test beds for exploring new aspects of superconductivity. A range of substituted ET derivatives is now becoming available.[7] The installation of a substituent on one of the ethylene bridges forms a stereogenic centre, and a number of racemic monosubstituted ET donors have been prepared, for example with sidechains terminating in amino[8] or amido[9] groups, *e.g.* **2** and **3**, or a long hydrocarbon chain,[10] *e.g.* **4**. The enantiopure ester **5**[11] has also been reported. Disubstituted and tetrasubstituted derivatives *e.g.* the enantiopure dimethyl-ET[12] **6** and its *meso*-isomer,[12] enantiopure tetramethyl-ET[13] **8** and racemic dichloro-ET[14] **7** as well as materials with additional ring systems such as **9**[15] have been prepared. However, care is necessary to avoid preparing mixtures of stereoisomers when each "end" of the ET molecule is substituted.[7] A number of interesting properties are emerging. Thus, a 2 : 1 superconducting perchlorate salt of enantiopure dimethyl-ET **6** (T_c = 3.0 K, 5.0 kbar) was reported by Hilti, Zambounis *et al.*, while a 2 : 1 hexafluorophosphate superconducting salt was obtained from the *meso*-isomer of this donor (T_c = 4.3 K, 4.0 kbar) by Mori *et al.*[12] Troitksy has used the hexadecyl-ET **4** to prepare conducting thin films.[16] New ET derivatives containing metal binding sites such as **10** with potential for preparing bifunctional materials with magnetic metal ions,[17,18] and an enantiopure donor **11** derived from (−)-β-pinene, have recently been prepared.[11] Cross-coupling reactions have been utilised to prepare substituted derivatives of the ethylenedithio-TTF system **12**.[19] Furthermore, substituted derivatives of selenium-containing donors, such as BETS[20] **13**, may soon become available following developments in synthetic approaches,[21] which will be of interest since some BETS radical cation salts have electrical properties which can be modified by an external magnetic field.[20]

Here we describe the synthesis of a range of ET donors carrying between one and eight hydroxyl groups. Introduction of hydroxyl groups on to a donor molecule brings not only the possibility of hydrogen bonding in the radical cation salts to anchor the anions in unique sites and orientations, but also provides a point for attachment of further functionality. In the TTF series mono-, di- and tetra-(hydroxymethyl) derivatives have been reported,[22–24] hydrogen bonding to anions in their radical cation salts has been observed,[24] and they have been utilised in the construction of more complex systems.[25] We and others have reported synthetic routes to racemic hydroxymethyl-ET **14**,[18,26,27] the cheapest and most efficient using the acetyl protecting group, and we have also synthesized the enantiopure form.[28] A number of semiconducting microcrystalline 2 : 1 radical cation salts of racemic **14** have been prepared.[26] Routes to the ET donor with *cis*-oriented hydroxymethyl groups **15**,[27] a stereoisomeric mixture of the tetrakis(hydroxymethyl)-ET **16**[29] and donors with expanded outer rings substituted with hydroxyl or hydroxymethyl groups

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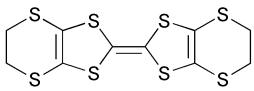

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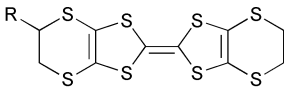
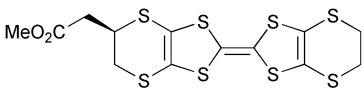


2 R = CH_2NH_2; 3 R = CH_2CONH_2
4 R = n-$C_{16}H_{33}$



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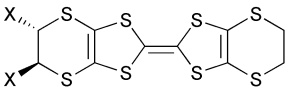
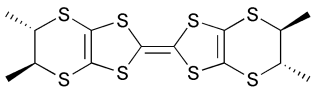


6 X = Me
(+/-) 7 X = Cl



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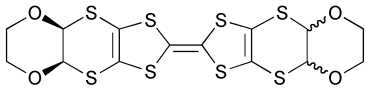

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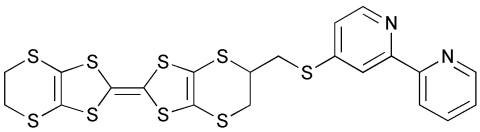

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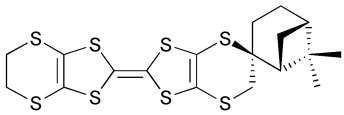

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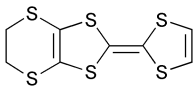

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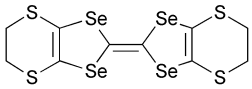

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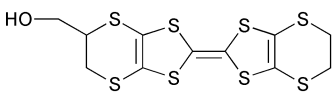
17 and **18**[30,31] have been reported. Two radical cation salts of bis(hydroxymethyl)-substituted materials have been described: $(\mathbf{15})_2$Cl and $(\mathbf{17})_2I_3$. In the former[27] the chloride is hydrogen bonded by hydroxyl groups from three donors, and lies between stacks of donors, while in the latter[32] the donors hydrogen bond with each other while the triiodides lie in isolated pockets. Here we describe, with experimental details, syntheses of racemic hydroxyethyl-ET **19** and *trans*-bis(hydroxymethyl)-ET **20**, the first synthesis of a single diastereoisomer of the tetrol tetrakis(hydroxymethyl)-ET, the *cis*,*trans* isomer **21**, and the syntheses of the enantiopure tetrol **22** and octol **23**, with the aim of making these new interesting donors accessible to the materials chemistry community.

Discussion

Preparation of hydroxyethyl-ET 19

The general approach in these syntheses is illustrated by the synthesis of hydroxyethyl-ET, HEET, **19**. The synthetic routes rely on the cyclisation of the trithione **24** with the appropriate alkene, a reaction first used by Neilands.[33] Refluxing but-3-en-1-ol with trithione **24** in toluene gave the thione **25** in 83% yield, followed by protection of the hydroxyl group as an acetate to give **26**, which was necessary for a successful subsequent cross-coupling reaction. Thione sulfur/oxygen exchange gave oxo compound **27**, which was cross-coupled with the unsubstituted thione **28**



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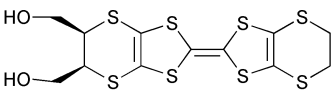

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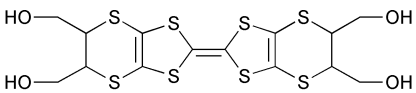

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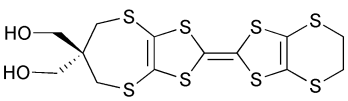

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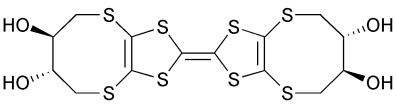

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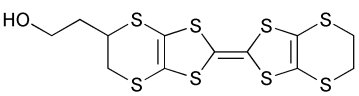

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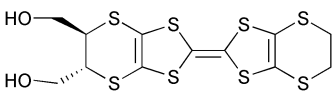

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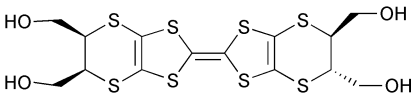

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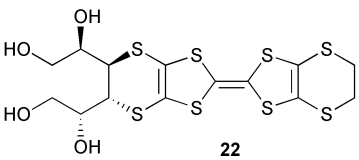

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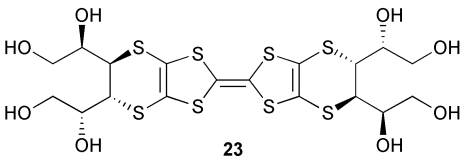

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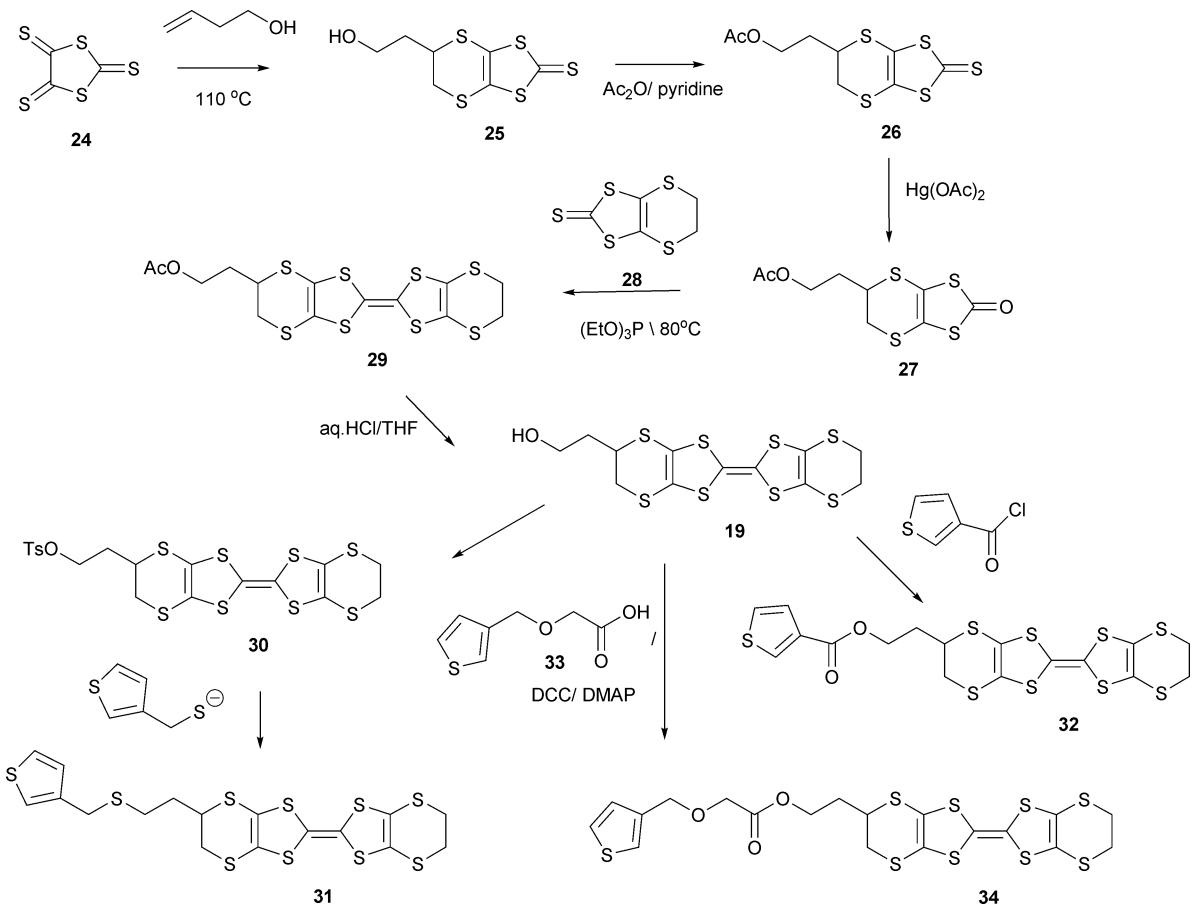

Scheme 1

to give the protected donor **29** in 54% yield. Hydrolysis gave HEET **19** in five steps with an overall yield of 14% (Scheme 1). Both hydroxymethyl-ET **14**[18] and HEET **19** have been functionalised either by ester formation or by tosylation and substitution. For example, HEET forms ester **32** with thiophene-3-carbonyl chloride and ester **34** with the thiophene-containing carboxylic acid **33** in the presence of DCC/DMAP, and its tosylate **30** is substituted with thiophene-3-methylthiolate to give sulfide **31**.

Preparation of *trans-vic*-bis(hydroxymethyl)-ET 20

The ET derivative with two vicinal *trans*-oriented hydroxymethyl groups was prepared in a similar way. Cyclisation of trithione **24** with the *trans*-but-2-en-1,4-diol, which was prepared from butyn-1,4-diol by reduction with lithium aluminium hydride,[34] gave diol **35** in 41% yield. Protection of hydroxyl groups as acetates, to give **36**, was followed by the standard three steps of (a) sulfur/oxygen exchange to give oxo compound **37**, (b) cross-coupling with unsubstituted thione **28** to give the protected donor **38** in 55% yield, and (c) deprotection to give the *trans* diol **20** in an overall yield of 17% (Scheme 2). The different disposition of the hydroxymethyl groups, compared to the *cis* isomer **15**, is expected to affect the structures of its radical cation salts with anions which can act as hydrogen bond acceptors.

Preparation of *cis*,*trans*-tetrakis(hydroxymethyl)-ET 21

Tetrakis(hydroxymethyl)-substituted ETs are very attractive donors because of the hydrogen bonding potential at both "ends" of the molecule. However, there are five possible stereoisomers depending on whether the two groups at each end of the molecule lie *cis* or *trans*, **41–45** (R = CH_2OH) (Scheme 3), and two of these stereoisomers (**41** and **45**) are racemic mixtures. It is important to develop syntheses of individual stereoisomers, since electrocrystallisation of a stereoisomeric mixture is a strategy fraught with problems; identification of the product relies on X-ray crystallography to determine which stereoisomer or stereoisomers are present,[35] assuming that all crystals have the same composition of course. An outline of the stereochemical consequences of various coupling strategies is given in Scheme 3. Homo-coupling of a racemic *trans*-disubstituted oxo compound **39** will give a racemic mixture of the tetrasubstituted ET **41** from self-coupling of each enantiomer of **39**, as well as a *meso* compound **42** arising from coupling of the two opposite enantiomers. Homo-coupling of a *cis*-disubstituted oxo compound **40** will give diastereomeric products **43** and **44**. In both cases, separation of the products is likely to be extremely difficult. Homo-coupling of one enantiomer of the *trans* oxo compound **39** would yield one enantiomer of the all-*trans* isomer **41**, but attempts to prepare the appropriate single enantiomer of the *trans* oxo compound **42** (R = CH_2OH) have so far been unsuccessful. The fifth stereoisomer **45** is the product of

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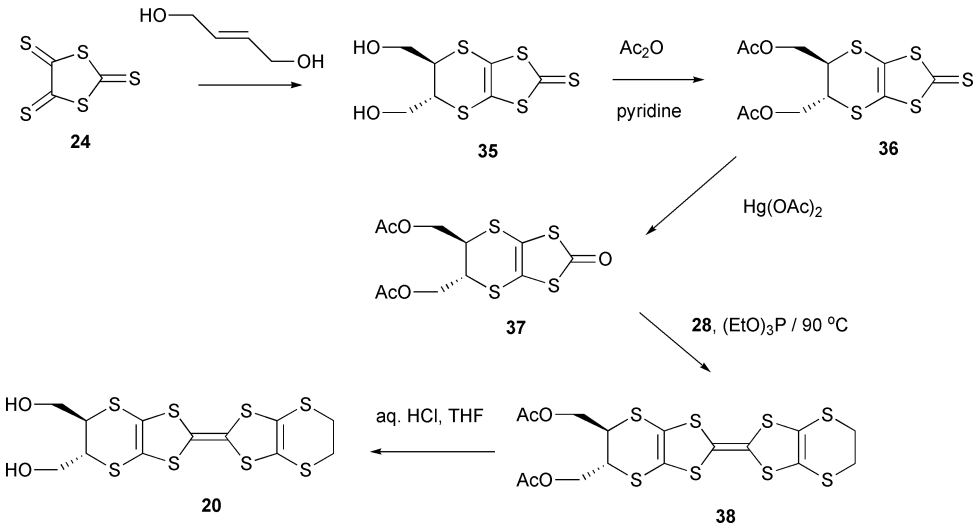


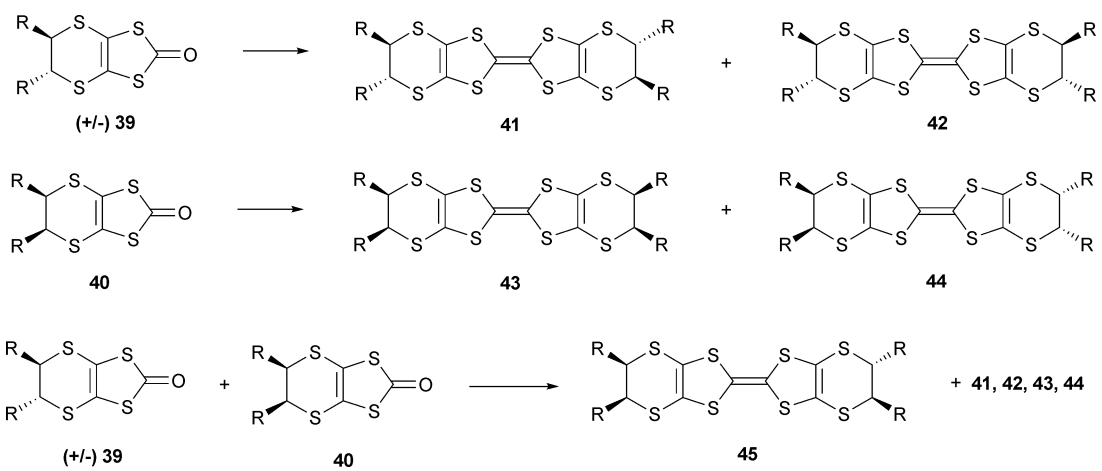
Scheme 2

cross-coupling of the *cis*- and *trans*-disubstituted oxo compounds **39** and **40**, but is accompanied by all other homo-coupled products.

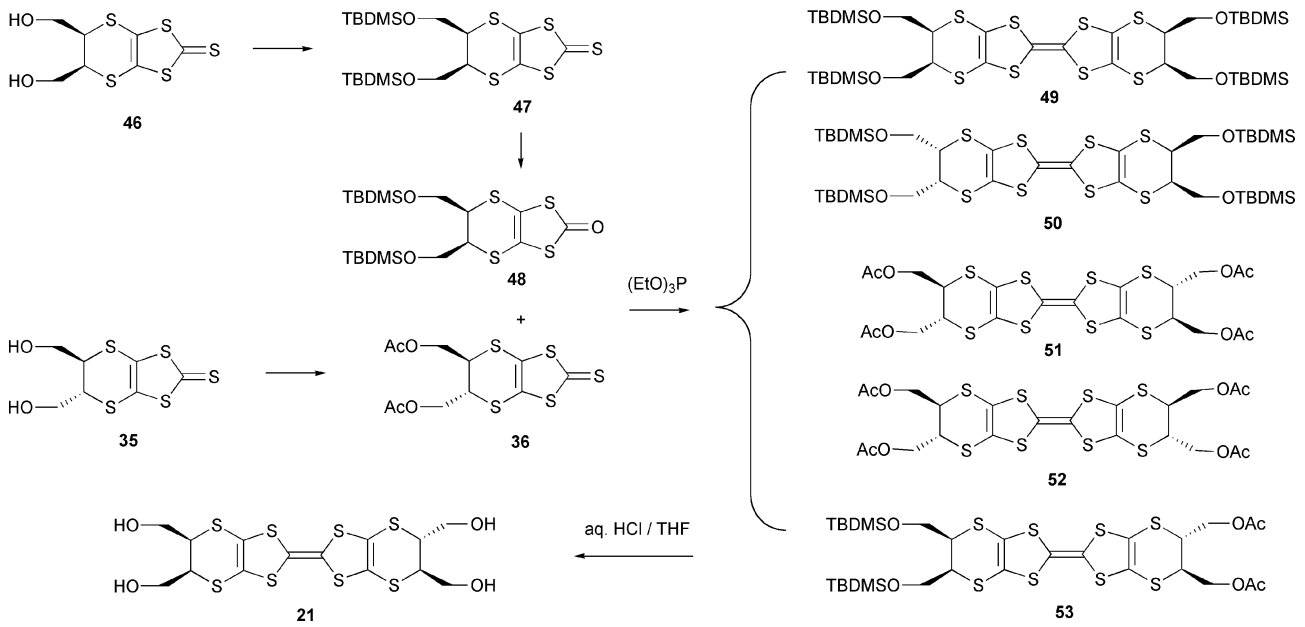
However, we have now developed a strategy for isolation of this last stereoisomer *cis*,*trans*-tetrakis(hydroxymethyl)-ET **21**. The overall synthetic plan is shown in Scheme 4. The key step is the protection of the hydroxyl groups of the *cis* and *trans* compounds for coupling with groups of quite different polarities. Thus, hydroxyl groups of the *cis*-bis(hydroxymethyl)thione **46** were protected with two BTDMS groups to give thione **47**,[27] which was converted to its oxo compound **48**. The hydroxyl groups of the *trans*-bis(hydroxymethyl)thione **35** were protected as acetates to give thione **36**. Cross-coupling of *cis*- and *trans*-compounds **48** and **36** in triethyl phosphite gave three sets of materials: the desired cross-coupled material **53** (2 × TBDMS, 2 × acetyl O-protecting groups) and the two pairs of homo-coupled materials: **49** and **50** (4 × TBDMS O-protecting groups) and **51** and **52** (4 × acetyl O-protecting groups). The three groups of materials were separated by chromatography. The cross-coupled product, with two protecting groups of each type, runs between the two sets of homo-coupled products which each carry four protecting groups of the same type. Finally, the tetrol **21** was prepared by hydrolysis of the protecting groups of **53** with aqueous 20% HCl in THF. We believe this principle of using two protecting groups of quite different polarities will find application in the synthesis of further polysubstituted donors.

Preparation of enantiopure tetrol and octol donors 22 and 23

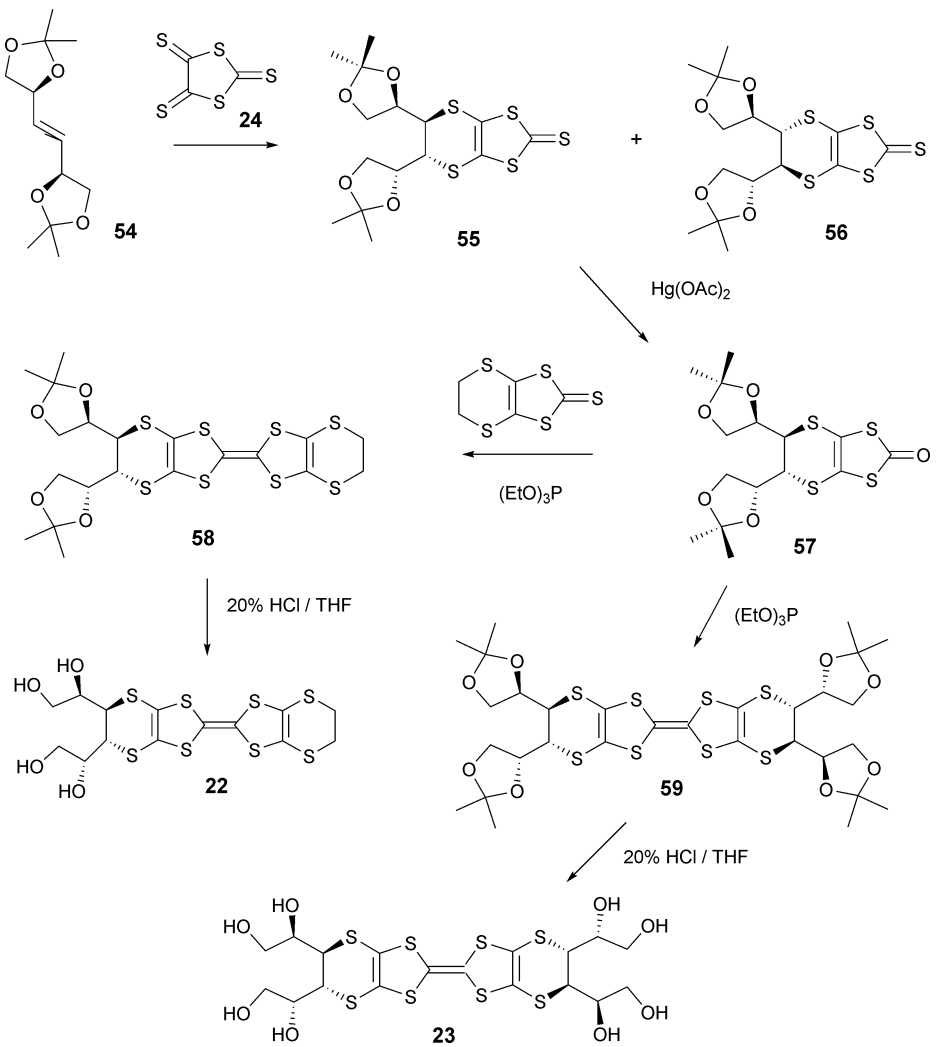
We have already reported the total diastereoselectivity of the reactions of the trithione **24** with enantiopure alkenes (−)-α-pinene, (−)-β-pinene and (+)-2-carene.[11] Encouraged by this, we extended the study to the structurally less complex enantiopure alkene **54** (Scheme 5) which has two stereocentres adjacent to the double bond and four protected hydroxyl groups and which is readily prepared from D-mannitol.[36] Trithione **24** reacted with this alkene to give major (31%) and minor (5%) 1 : 1 addition products which were assigned structures **55** and **56** respectively, based on the X-ray crystal structure of the minor isomer **56** (Fig. 1). Thus, the major product is formed by addition of trithione **24** to the *Si* face of enantiopure alkene **54** as shown in Fig. 2, while the minor adduct is formed by addition to the *Re* face. Molecular mechanics studies indicated there was no strong conformational preference



Scheme 3



Scheme 4



Scheme 5

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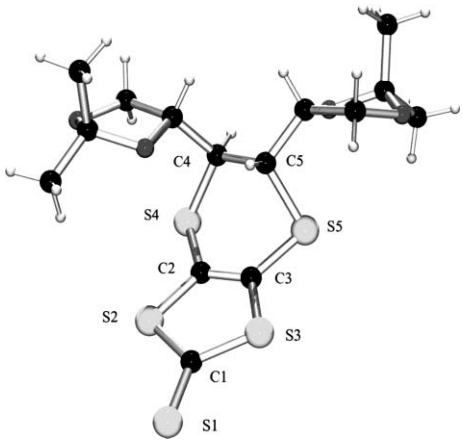


Fig. 1 Molecular structure of minor diastereomer **56**.

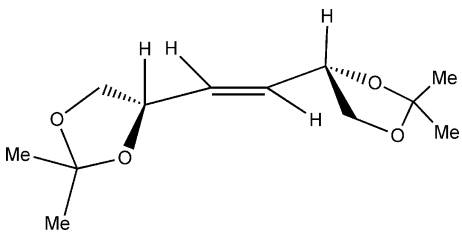
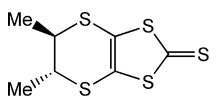


Fig. 2 Preferred conformation of alkene **54** with the *Si* face upwards.

for rotation about the bonds between the alkene and each cyclic ketal, with a small energy minimum for the conformation shown in Fig. 2.

The X-ray structure of the minor product **56** shows that the dithiin ring takes up a twisted boat conformation with both ring sp^3 carbon atoms strongly displaced to the same side of the plane defined by the other atoms of the fused ring system but with C5 displaced by more than C4 (C4: by 1.277(4), C5 by 1.486(5) Å). The torsions about the dithiin sp^2 C–S bonds are −48.8(5) and 52.0(5)°, and the twist in the boat structure is indicated by the largest torsion in this ring about the C5–S5 bond: −66.3(4)°, much larger than that of 28.4(5)° for the C4–S4 bond. The *trans* arrangement of the dioxolane rings means that one lies over the organosulfur ring system and the other lies away from it. Each dioxolane ring adopts an envelope conformation with the flap at the carbon atom between the oxygen atoms. The best planes of these rings lies at 40.3(2) and 50.7(2)° to the best plane through the planar portion of the organosulfur system. There are distinct differences in the chemical shifts of the carbon atoms in the dithiin ring for the major and minor diastereoisomers **55** and **56**. The major isomer exhibits chemical shifts for the sp^3 C atoms at δ_C 44.3 and for the sp^2 C atoms at δ_C 118.9, similar to those of other *trans*-disubstituted derivatives *e.g.* the dimethyl derivative **60** (δ_C 43.5 and 120.4) whose solid-state conformation lies between a half-chair and an envelope.[37] In contrast, for the minor diastereomer the shifts of the corresponding carbon atoms are larger: δ_C 51.7 and 128.3. The *trans* diester **61**, which like the minor isomer also



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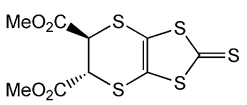

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Table 1 Cyclic voltammetry data for selected donors[a]

Compound	E_1	E_2
1	0.51	0.94
19	0.49	0.90
20	0.50	0.88
21	0.52	0.86
22	0.52	0.85
58	0.55	0.93
59	0.55	0.89

[a] Measured relative to Ag/AgCl at a platinum electrode in dichloromethane containing 0.1 M Bu_4NPF_6 as charge carrier and using a 100 mV s^{-1} scan.

shows a boat conformation in the solid state, has corresponding shifts at δ_C 50.2 and 129.9.[38] These larger shifts may relate in part to the poorer conjugation of the dithiin S atoms with the dithiole ring when the former has the boat conformation.

The major product **55** was converted to its oxo compound **57** with mercuric acetate and coupled to the unsubstituted thione **28** using triethyl phosphite to give the protected donor **58** in 35% yield after chromatography. Finally, deprotection with 2 M HCl in THF yielded the enantiopure tetrol **22** in 94% yield. Furthermore, self-coupling of the oxo compound **57** in triethyl phosphite furnished the donor bearing four ketal groups **59** in 60% yield, which could be deprotected in a similar way to give the enantiopure octol **23**.

The oxidation potentials of the new hydroxyl-substituted donors, measured in dichloromethane, indicate that the overall pattern of two reversible oxidations is retained (Table 1), though the octol **23** was completely insoluble in this solvent, and measurements in THF did not indicate a reversible system. We are now investigating the electrocrystallisation of these materials. Of particular interest will be to see how the interaction of the hydroxyl groups with the anions control the solid-state structures of the radical cation salts.

Conclusion

We have reported syntheses of a series of ET-derivatives carrying one, two, four and eight hydroxyl groups, two of them in enantiopure form. Molecules **22** and **23** are particularly attractive donors, since, apart from the potential for having chiral hydrogen bonding networks in their radical cation salts, these donors are starting materials for preparing dendrimeric materials. These single enantiomers will also provide important substrates for investigating the influence of chirality on electrical and magnetic properties. The second enantiomer of **23** will be available from the other enantiomer of alkene **54**, and the racemate is available by mixing equal amounts of the two enantiomers, a rare case where it is more work to prepare the racemate than the enantiomer. Rikken has reported magnetochiral anisotropy in the conductivity of carbon nanotubes,[39] and our donors will provide a test bed for investigating the effect of chirality on the electrical properties of organosulfur donors. Furthermore, the diastereoselectivity of the cycloaddition of thione **24** with alkene **54** is a very encouraging result, suggesting that cycloadditions of trithione **24** with further enantiopure alkenes will be a key step in designing and preparing further enantiopure donors.

Experimental

General

NMR spectra were measured on a JEOL JNM-EX270 spectrometer at 270 MHz for ^{1}H and at 67.8 MHz for ^{13}C using $CDCl_3$ as solvent and tetramethylsilane (TMS) as standard unless otherwise stated, and measured in ppm downfield from TMS with coupling constants reported in Hz. IR spectra were recorded on a PerkinElmer Spectrum RX 1 FT-IR spectrometer, and are reported in cm^{-1}. Optical rotation data were measured on a PerkinElmer 241 polarimeter. Mass spectra were recorded at the EPSRC Mass Spectrometry Centre. Chemical analysis data were obtained from Mr T. Spencer, University of Nottingham. An X-ray diffraction dataset was measured by the EPSRC National Crystallography Service at Southampton University. Flash chromatography was performed on 40–63 silica gel (Merck).

5,6-Dihydro-5-(2′-hydroxyethyl)-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-thione, 25. 3-Buten-1-ol (7.00 g, 104.4 mmol) and trithione **24**[40] (8.00 g, 40.8 mmol) were refluxed in toluene (400 ml) for 4 h. After cooling to room temperature the reaction mixture was filtered, and the solid washed with ethanol. Combined washings and filtrate were evaporated and the residue purified by flash chromatography (ethyl acetate) to furnish **25** as an orange oil (8.84 g, 83.0%), which solidified on standing; mp 52–53 °C; δ_H: 3.88 (3H, m, 2′-CH_2 and 5-*H*), 3.46 (1H, dd, $J = 13.4, 2.8$, 6-H_α), 3.22 (1H, dd, $J = 13.4, 6.7$, 6-H_β), 2.02 (2H, m, 1′-CH_2), 1.52 (1H, s, O*H*); δ_C: 207.7 (*C*=S), 121.9, 121.5 (3a- & 7a-*C*), 59.3 (2′-*C*H$_2$), 39.8 (5-*C*), 37.1 (6-*C*), 34.9 (1′-*C*H$_2$); ν_{max} (thin film): 3386, 2924, 1483, 1412, 1293, 1057, 890; found C, 31.3, H, 2.9%, $C_7H_8OS_5$ requires C, 31.3, H, 3.0%.

5,6-Dihydro-5-(2′-acetyloxyethyl)-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-thione, 26. Acetic anhydride (4 ml, 36.3 mmol) was added to a solution of **25** (8.84 g, 33.9 mmol) in pyridine (50 ml) at room temperature and then stirred at 70 °C for 12 h. Water (300 ml) was added and the mixture extracted with CH_2Cl_2 (3 × 100 ml). The organic solution was washed consecutively with 0.5 M HCl solution (3 × 100 ml) and H_2O (100 ml), dried (Na_2SO_4) and evaporated to yield **26** as a brown oil (8.86 g, 86.0%); δ_H: 4.25 (2H, m, 2′-CH_2), 3.73 (1H, m, 5-*H*), 3.43 (1H, dd, $J = 13.3, 3.0$, 6-H_α), 3.20 (1H, dd, $J = 13.3, 6.8$, 6-H_β), 2.14 (2H, m, 1′-CH_2), 2.05 (3H, s, CH_3); δ_C: 207.7 (2-*C*), 170.7 (*C*=O) 122.0, 121.7 (3a- & 7a-*C*), 60.8 (2′-*C*H$_2$), 39.7 (5-*C*), 34.6 (6-*C*), 33.8 (1′-*C*H$_2$), 20.9 (*C*H$_3$); ν_{max} (thin film): 2955, 1737, 1485, 1426, 1384, 1364, 1236, 1062, 890; found C, 34.8, H, 3.1%, $C_9H_{10}O_2S_5$ requires C, 34.8, H, 3.3%.

5,6-Dihydro-5-(2′-acetyloxyethyl)-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-one, 27. To a solution of **26** (8.86 g, 29.2 mmol) in $CHCl_3$ (100 ml) and glacial acetic acid (30 ml) was added mercuric acetate (15.02 g, 47.1 mmol). After 2 h stirring at room temperature the mixture was filtered. The filtrate was washed consecutively with saturated $NaHCO_3$ solution (3 × 100 ml) and water (100 ml), dried (Na_2SO_4) and evaporated to afford **27** as a light brown solid (5.65 g, 67.5%); mp 46–47 °C; δ_H: 4.23 (2H, m, 2′-CH_2), 3.74 (1H, m, 5-*H*), 3.45 (1H, dd, $J = 13.3, 2.7$, 6-H_α), 3.20 (1H, dd, $J = 13.3, 6.7$, 6-H_β), 2.14 (2H, m, 1′-CH_2), 2.03 (3H, s, CH_3); δ_C: 188.3 (2-*C*), 170.7 (CH$_3$*C*=O), 112.4, 112.3 (3a- & 7a-*C*), 60.8 (2′-*C*H$_2$), 41.2 (5-*C*), 35.8 (6-*C*), 33.8 (1′-*C*H$_2$), 20.8 (*C*H$_3$); ν_{max} (KBr): 2967, 1729, 1670, 1634, 1509, 1464, 1425, 1398, 1368, 1247, 1049, 895, 767, 469; found C, 36.7, H, 3.3%, $C_9H_{10}O_3S_4$ requires C, 36.7, H, 3.4%.

(2-Acetyloxyethyl)-ET, 29. A mixture of oxo compound **27** (2.83 g, 9.90 mmol) and unsubstituted thione **28** (4.43 g, 19.8 mmol) were heated in triethyl phosphite to 80 °C under N_2 for 5 h to give an orange solution. Triethyl phosphite was removed by distillation *in vacuo* and the residue purified by flash chromatography (5 : 1 cyclohexane–ethyl acetate) to yield **29** as a red–orange solid (2.50 g, 54.5%); mp 109–110 °C; δ_H: 4.23 (2H, m, 2′-CH_2), 3.64 (1H, m, 5-*H*), 3.34 (1H, dd, $J = 13.1, 3.2$, 6-H_α), 3.32 (4H, s, 5″- & 6″-H_2), 3.32 (1H, dd, $J = 13.1, 6.5$, 6-H_β), 2.05 (5H, m, CH_3 & 1′-CH$_2$); δ_C: 170.7 (*C*=O) 113.9 & 113.0 (sp^2-*C*), 61.2 (1′-*C*H$_2$), 40.1 (5-*C*), 35.3 (6-*C*), 33.7 (1′-*C*H$_2$), 30.2 (5″- & 6″-*C*), 20.9 (*C*H$_3$); ν_{max}(KBr): 2955, 2920, 1731, 1365, 1239, 1039, 905, 772, 668; found C, 35.8, H, 3.0%, $C_{14}H_{14}O_2S_8$ requires C, 35.7, H, 3.0%.

(2′-Hydroxyethyl)-ET, 19. A solution of **29** (0.65 g, 1.40 mmol) in THF (10 ml) and 20% HCl solution (5 ml) was stirred under N_2 for 48 h. The solution was neutralised by the addition of solid $NaHCO_3$. The organic layer was collected, dried (Na_2SO_4) and purified by flash chromatography (2 : 1 cyclohexane–ethyl acetate) to afford **19** (0.31 g, 51%) as a bright orange powdery solid; mp 141–142 °C; δ_H: 4.69 (1H, t, $J = 5.1$, O*H*), 3.81 (1H, m, 5-*H*), 3.55 (2H, m, 2′-CH_2), 3.45 (1H, dd, $J = 13.2, 3.0$, 6-H_α), 3.38 (4H, s, 5″-, 6″-H_2), 3.27 (1H, dd, $J = 13.2, 6.5$, 6-H_β), 1.84 (2H, m, 1′-CH$_2$); δ_C: 115.1, 115.0 & 114.4 (sp^2-*C*), 59.8 (2′-*C*H$_2$), 42.5 (5-*C*), 39.5 (6-*C*), 36.9 (1′-*C*H$_2$), 31.2 (5″- & 6″-*C*); ν_{max} (KBr): 3450, 2922, 1652, 1458, 1280, 1046, 767; found C: 33.7, H: 3.0%, $C_{12}H_{12}OS_8$ requires C: 33.6, H: 2.8%.

(2′-Tosyloxyethyl)-ET, 30. Hydroxyethyl-ET **19** (0.20 g, 0.47 mmol) and tosyl chloride (0.36 g, 1.88 mmol) were stirred together in dry pyridine (2 ml) under nitrogen for 2 h. The resulting solution was diluted with chloroform (25 ml), absorbed on silica and purified by flash chromatography (2 : 1 cyclohexane–ethyl acetate) to give **30** (0.17 g, 64%) as an orange solid, mp 90 °C; δ_H: 7.78 (2H, d, $J = 8.2$, Ar-H_2), 7.36 (2H, d, $J = 8.2$, Ar-H_2), 4.18 (2H, t, $J = 5.7$, -CH_2O), 3.63 (1H, m, 5-*H*), 3.33 (1H, dd, $J = 3.1, 13.3$, 6-H_α), 3.27 (4H, s, 5″-,6″-H_2), 2.99 (1H, dd, $J = 5.7, 13.3$, 6-H_β), 2.45 (Ar-CH_3), 2.03 (2H, m, 1′-CH_2); δ_C (DMSO-d$_6$): 145.1, 132.3, 130.0, 127.8 (Ar-C_6), 113.7, 113.0, 112.1 (sp^2-*C*), 67.0 (2′-*C*), 38.3 (5-*C*), 34.8 (6-*C*), 33.6 (1′-*C*H$_2$), 30.1 (5″- & 6″-*C*), 21.6 (*C*H$_3$); ν_{max} (KBr): 2922, 1596, 1410, 1349, 1286, 1187, 1172, 1094, 966, 905, 811, 769, 663, 553; *m/z* (CI): 583 ([M + 1]$^+$, 10), 411 ([M − TsO]$^+$, 100); HRMS (ES): found [M$^+$] 582.8822, $C_{19}H_{18}O_3S_9$ requires 582.8820.

Thiophen-3-ylmethylthioethyl-ET, 31. To a solution of sodium metal (0.03 g, 1.2 mmol) in dry methanol (5 ml) under nitrogen and in the dark was added a solution of thiophene-3-methylthiol[41] (0.12 g, 1 mmol) in dry THF (10 ml). After 10 min stirring, a solution of tosylate **30** (0.30 g, 0.52 mmol) in dry THF (20 ml) was added and the resulting mixture stirred for 20 h. The mixture was partitioned between DCM and water and the organic layer collected, dried over $MgSO_4$ and purified by flash chromatography (8 : 1 cyclohexane–ethyl acetate) to yield **31** (0.21 g, 71%) as an orange solid; mp 159–162 °C; δ_H: 7.30 (dd, 1H, $J = 3.0, 5.0$, 4″-*H*), 7.10 (dd, 1H, $J = 1.2, 3.0$, 5″-*H*), 7.07 (dd, 1H, $J = 1.2, 5.0$, 2″-*H*), 3.74 (s, 2H, SCH_2Ar), 3.65 (m, 1H, 5-*H*), 3.28 (m, 5H, 6$_\alpha$-, 5′-,

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6′-*H*), 2.95 (dd, 1H, $J = 6.4, 13.1$, 6_β-*H*), 2.58 (m, 2H, SCH_2CH$_2$), 1.94 (m, 2H, SCH$_2$CH_2); δ_C: 138.4 (3″-*C*), 128.0 (2″-*C*), 126.3 (5″-*C*), 122.4 (4″-*C*), 113.0, 112.9, 111.7, 111.6 (sp^2-*C*), 42.0 (5-*C*), 35.1 (S*C*H$_2$Ar), 33.8 (6-*C*), 30.9 (S*C*H$_2$CH$_2$), 30.1 (5′-, 6′-*C*), 28.4 (SCH$_2$*C*H$_2$); ν_{max} (KBr): 2916, 1408, 1284, 1233, 886, 773, 726, 678, 616; *m/z* (EI): 540 ([M]$^+$, 20%), 236 (55%), 224 (100%); HRMS (EI): found [M$^+$] 539.8454, $C_{17}H_{16}S_{10}$ requires 539.8454.

Thiophene-3-carboxylic acid, HEET ester, 32. To a solution of HEET **19** (0.16 g, 0.38 mmol) in dry THF (10 ml) was added triethylamine (2 ml) and thiophene-3-carbonyl chloride (0.11 g, 0.77 mmol), which had been prepared from the carboxylic acid[42] and thionyl chloride. This mixture was stirred for 12 h, concentrated and purified by flash chromatography (10 : 1 cyclohexane–ethyl acetate) to yield **32** (0.13 g, 62%) as an orange solid; mp 125–128 °C; δ_H: 8.11 (dd, 1H, $J = 1.1, 3.1$, 2″-*H*), 7.51 (dd, 1H, $J = 5.0, 1.1$, 5″-*H*), 7.32 (dd, 1H, $J = 3.1, 5.0$, 4″-*H*), 4.46 (m, 2H, CH_2O), 3.66 (m, 1H, 5-*H*), 3.40 (dd, 1H, $J = 3.1$ 13.1, 6-H_α), 3.27 (s, 4H, 5′-, 6′-H_2), 3.14 (dd, 1H, $J = 6.4, 13.1$, 6-H_β), 2.22 (m, 2H, 5-CH_2); δ_C: 162.4 (*C*=O), 133.1 (4″-*C*), 133.0 (3″-*C*), 127.8 (2″-*C*), 126.2 (5″-*C*), 113.8, 113.0, 112.9, 111.4 (sp^2-*C*), 61.4 (*C*H$_2$O), 40.3 (5-*C*), 35.3 (6-*C*), 33.9 (5-*C*H$_2$), 30.1 (5′-, 6′-*C*); ν_{max} (KBr): 3000, 2909, 1703, 1518, 1414, 1266, 1189, 1109, 1008, 824, 771, 752, 700, 502; *m/z* (EI): 537.8 ([M]$^+$, 100%); HRMS (EI): found 537.8463 [M]$^+$, $C_{17}H_{14}O_2S_9$ requires 537.8480.

Thiophen-3-ylmethoxyacetic acid, HEET ester, 34. To a solution of HEET **19** (0.20 g, 0.47 mmol), thiophen-3-ylmethoxyacetic acid[43] (0.08 g, 0.47 mmol) and 4-dimethylaminopyridine (5 mg) in dry dichloromethane (10 ml) was added *N*,*N*′-dicyclohexylcarbodiimide (0.13 g, 0.61 mmol). This was stirred for 20 h at room temperature, after which the mixture was concentrated and purified by chromatography (5 : 1 cyclohexane–ethyl acetate) to yield **34** (0.15 g, 56%) as an oily orange solid; δ_H: 7.25 (dd, 1H, $J = 3.0, 5.0$, 5″-*H*), 7.20 (br s, 1H, 2″-*H*), 7.03 (br d, 1H, $J = 5.0$, 4″-*H*), 4.57 (s, 2H, OCH_2Ar), 4.25 (m, 2H, CH$_2$CH_2O), 4.03 (s, 2H, C(O)CH_2O), 3.55 (m, 1H, 5-*H*) 3.29 (dd, 1H, $J = 3.0, 13.1$, 6-H_α), 3.21 (s, 4H, 5′-, 6′-H_2), 3.00 (dd, 1H, $J = 6.2, 13.1$, 6-H_β), 2.02 (d, 2H, $J = 6.4$, 5-CH_2); δ_C: 170.0 (*C*=O), 137.9 (3″-*C*), 127.3 (2″-*C*), 126.2 (5″-*C*), 123.7 (4″-*C*), 113.7, 112.9, 112.5, 111.8 (sp^2-*C*), 68.3 (O*C*H$_2$Ar), 66.8 (C(O)*C*H$_2$O), 61.5 (CH$_2$*C*H$_2$O), 39.8 (5-*C*), 35.1 (6-*C*), 33.5 (5-*C*H$_2$), 30.0 (5′-, 6′-*C*); ν_{max} (KBr): 2916, 2853, 1747, 1659, 1456, 1415, 1275, 1192, 1155, 1119, 1010, 917, 885, 854, 766, 693; *m/z* (CI): 583 ([M]$^+$, 10%), 244 (100%); HRMS (EI): found 581.81737 [M]$^+$, $C_{19}H_{18}O_3S_9$ requires 581.8741.

***trans*-5,6-Bis(hydroxymethyl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-thione, 35.** A mixture of (*E*)-but-2-en-1,4-diol[34] (1.50 g, 17.0 mmol) and trithione **24** (2.23 g, 11.3 mmol) in toluene (220 ml) was refluxed for 5 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography (1 : 1 cyclohexane–ethyl acetate) to give **35** as a brown powdery solid (1.33 g, 41.2%); mp 110–112 °C; δ_H (MeOH-d$_4$): 3.80 (6H, m, 5-, 6-*H* & 2 × CH_2O); δ_C (MeOH-d$_4$): 209.5 (2-*C*), 122.7 (3a-, 7a-*C*), 64.9 (2 × *C*H$_2$OH), 45.4 (5-, 6-*C*); ν_{max} (KBr): 3260, 2931, 2872, 1485, 1459, 1070, 1041, 1019; found C, 29.6, H, 2.8%, $C_7H_8O_2S_5$ requires C, 29.6, H, 2.8%.

***trans*-5,6-Bis(acetyloxymethyl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-thione, 36.** Acetic anhydride (0.70 ml, 7.40 mmol) was added to a solution of **35** (1.05 g, 3.70 mmol) in pyridine (15 ml) at 0 °C and the mixture stirred at room temperature overnight. DCM (100 ml) and water (30 ml) were added. The mixture was shaken and the organic layer collected. This was washed sequentially with 1 M HCl (3 × 100 ml) and water (50 ml), dried (MgSO$_4$) and evaporated to yield **36** as a dark orange–brown oil (1.28 g, 94.1%); δ_H: 4.32 (4H, m, 2 × CH_2O), 3.74 (2H, m, 5, 6-*H*), 2.07 (6H, s, 2 × OCH_3); δ_C: 206.5 (2-*C*), 170.7 (2 × *C*=O) 118.8 (3a-, 7a-*C*), 64.7 (2 × *C*H$_2$O), 40.1 (5-, 6-*C*), 20.7 (2 × *C*H$_3$); ν_{max} (thin film): 2923, 1743, 1381, 1363, 1222, 1064, 1034; *m/z* (AP): 369 ([M + H]$^+$,100), 309 (5); HRMS (ES): found: 368.9419 (M + H)$^+$, $C_{11}H_{12}O_4S_5$ + H requires: 368.9417.

***trans*-5,6-Bis(acetyloxymethyl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-one, 37.** To a solution of **36** (0.15 g, 0.41 mmol) in CHCl$_3$ (10 ml) and glacial acetic acid (3 ml) was added mercuric acetate (0.19 g, 0.61 mmol). After 2 h stirring at room temperature the mixture was filtered. The filtrate was washed consecutively with saturated NaHCO$_3$ solution (3 × 10 ml) and H$_2$O (10 ml), dried (Na$_2$SO$_4$) and evaporated to afford **37** as a light brown oil (0.13 g, 90.6%); δ_H: 4.34 (4H, m, 2 × CH_2O), 3.72 (2H, m, 5-, 6-*H*), 2.04 (6H, s, 2 × CH_3); δ_C: 187.2 (2-*C*), 169.7 (2 × *C*=O) 109.6 (3a-, 7a-*C*), 64.5 (5-, 6-*C*H$_2$O), 41.2 (5-, 6-*C*), 20.4 (2 × *C*H$_3$); ν_{max} (thin film): 3025, 2943, 1744, 1692, 1644, 1507, 1440, 1381, 1364, 1222, 1035, 891, 755; *m/z* (AP): 352 ([M]$^+$,80), 293 (100); HRMS (ES): found: 369.9914 (M + NH$_4$)$^+$, $C_{11}H_{12}O_5S_4$ + NH$_4$ requires: 369.9911.

***trans*-*vic*-Bis(acetyloxymethyl)-ET, 38.** A mixture of oxo compound **37** (0.75 g, 2.13 mmol) and thione **28** (0.72 g, 3.20 mmol) were heated in triethyl phosphite (10 ml) to 90 °C under N$_2$ for 5 h to give an orange solution. Triethyl phosphite was removed by distillation *in vacuo* and the residue purified by flash chromatography (3 : 1 cyclohexane–ethyl acetate) to yield **38** as an orange solid (0.62 g, 55.1%); mp 122–123 °C; δ_H: 4.27 (2H, dd, $J = 11.2, 5.7$, 2 × CH_αO), 4.23 (2H, dd, $J = 11.2, 8.0$, 2 × CH_βO), 3.65 (2H, m, 5-, 6-*H*), 3.24 (4H, s, 5′-, 6′-H_2), 2.04 (6H, s, 2 × CH_3); δ_C: 170.2 (2 × *C*=O) 113.7, 110.2 (sp^2-*C*), 64.7 (2 × *C*H$_2$O), 40.6 (5-, 6-*C*), 30.0 (5′-,6′-*C*), 20.7 (2 × *C*H$_3$); ν_{max} (KBr): 2931, 1740, 1381, 1362, 1230, 1033, 909, 772; *m/z* (AP): 529 ([M + H]$^+$, 100), 357 (80); HRMS (ES): found: 528.8886 (M + H)$^+$, $C_{16}H_{16}O_4S_8$ + H requires: 528.8892.

***trans*-*vic*-Bis(hydroxymethyl)-ET, 20.** A solution of donor **38** (0.20 g, 0.38 mmol) in THF (20 ml) and 20% HCl solution (10 ml) was stirred under N$_2$ overnight. The solution was neutralised by the addition of solid NaHCO$_3$. The organic layer was collected, dried (Na$_2$SO$_4$) and evaporated to afford **20** (0.15 g, 89.2%) as a bright orange powdery solid; mp 150 °C (dec.); δ_H (MeOH-d$_4$): 3.65 (6H, m, 2 × C*H*CH_2), 3.25 (4H, s, 5′-, 6′-H_2); δ_C (MeOH-d$_4$): 114.8, 112.6 (sp^2-*C*), 65.0 (2 × *C*H$_2$O), 45.9 (5, 6-*C*), 31.1 (5′-, 6′-*C*); ν_{max} (KBr): 3401, 2919, 2861, 1451, 1417, 1298, 1167, 1026, 1005, 884, 773; *m/z* (AP): 445 ([M + H]$^+$, 100), 357 (51); HRMS (EI): found: 443.8605, $C_{12}H_{12}O_2S_8$ requires: 443.8603.

***cis*-5,6-Bis(hydroxymethyl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-thione, 46[29,33].** A mixture of *cis*-but-2-en-1,4-diol (1.70 ml, 20.4 mmol) and the trithione **24** (2.00 g, 10.2 mmol) in toluene (200 ml) was refluxed for 5 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography (1 : 1 cyclohexane–ethyl acetate) to give **5** as a

bright yellow powder (1.10 g, 38.0%); δ_H: 4.96 (2H, s, 2 × O*H*), 4.06 (4H, m, 5-, 6-*H* & 2 × CH_αO), 3.91 (2H, m, 2 × CH_βO); δ_C: 209.9 (2-*C*), 122.7 (3a-, 7a-*C*), 63.0 (2 × *C*H_2OH), 45.4 (5-, 6-*C*); ν_{max} (KBr): 3218, 2938, 1494, 1459, 1069, 1041, 1017, 894.

***cis*-5,6-Bis(*tert*-butyldiphenylsilyloxymethyl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-thione, 47.** To a solution of **46** (2.00 g, 7.04 mmol) in dry DMF (120 ml) was added sequentially imidazole (9.59 g, 140.8 mmol) and *tert*-butyldiphenylsilyl chloride (4.51 ml, 17.6 mmol). After stirring at room temperature overnight, water (100 ml) and dichloromethane (200 ml) were added, the dichloromethane layer separated, and the aqueous layer extracted twice more with dichloromethane (2 × 40 ml). The combined organic solution was washed sequentially with ice-cold HCl (3 M, 3 × 50 ml) and water (50 ml) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by flash chromatography (dichloromethane) to afford **47** as an orange oil (2.67 g, 49.8%); δ_H: 7.75 (8H, m, Ar-H_8), 7.50 (12H, m, Ar-H_{12}), 4.06 (6H, m, 2 × CH_2O, 5-, 6-*H*), 1.15 (18H, s, 2 × C(CH_3)$_2$); δ_C: 207.8 (2-*C*), 135.4, 132.4, 129.9, 127.8 (Ar-C_{24}), 121.4 (3a-, 7a-*C*), 63.5 (2 × *C*H_2O), 47.9 (5, 6-*C*), 26.7 (2 × C(*C*H_3)$_3$), 19.0 (2 × *C*(CH_3)$_3$); ν_{max} (thin film): 2933, 2922, 2856, 1720, 1470, 1427, 1273, 1113, 1067, 823, 739, 701, 614; *m*/*z* (AP): 778 ([M + H_2O]$^+$, 38), 249 (100); HRMS (EI): found: 760.1473, $C_{39}H_{44}O_2S_5$ Si_2 requires: 760.1483.

***cis*-5,6-Bis(*tert*-butyldiphenylsilyloxymethyl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-one, 48.** To a solution of thione **47** (2.50 g, 3.28 mmol) in $CHCl_3$ (60 ml) and glacial acetic acid (20 ml) was added mercuric acetate (1.57 g, 4.92 mmol). After 2 h stirring at room temperature the mixture was filtered. The filtrate was washed consecutively with saturated $NaHCO_3$ solution (3 × 100 ml) and H_2O (100 ml), dried (Na_2SO_4) and evaporated to afford **48** as an orange oil (2.37 g, 97.0%); δ_H: 7.80 (8H, m, Ar-H_8), 7.49 (12H, m, Ar-H_{12}), 4.10 (6H, m, 2 × CH_2O, 5-, 6-*H*), 1.18 (18H, s, 2 × C(CH_3)$_3$); δ_C: 188.5 (2-*C*), 135.2, 132.3, 129.6, 127.5 (Ar-C_{24}), 111.3 (3a-, 7a-*C*), 63.5 (2 × *C*H_2O), 48.9 (5-, 6-*C*), 26.5 (2 × C(*C*H_3)$_3$), 18.9 (2 × *C*(CH_3)$_3$); ν_{max} (thin film): 3075, 2955, 2932, 2856, 1682, 1627, 1471, 1427, 1112, 823, 738, 700; found C, 62.5, H, 5.8%, $C_{39}H_{44}O_3S_4Si_2$ requires C, 62.9, H, 6.0%.

***cis*-Bis(*tert*-butyldiphenylsilyloxymethyl)-*trans*-bis(acetyloxymethyl)-ET, 53.** A mixture of oxo compound **47** (2.37 g, 3.19 mmol) and thione **36** (1.20 g, 3.26 mmol) were heated in triethyl phosphite (30 ml) to 90 °C under N_2 for 5 h to give an orange solution. Triethyl phosphite was removed by distillation *in vacuo* and the residue purified by flash chromatography (5 : 1 cyclohexane–ethyl acetate) to yield **53** as an orange oil (0.68 g, 20.0%) from the second orange band; δ_H: 7.70 (8H, m, Ar-H_8), 7.40 (12H, m, Ar-H_{12}), 4.33 (2H, m, 5′, 6′-*H*), 3.80 (10H, m, 5-, 6-*H* & 5-, 6-, 5′, 6′-CH_2O), 2.10 (6H, s, 2 × COCH_3), 1.01 (18H, s, 2 × C(CH_3)$_2$); δ_C: 170.2 (2 × *C*=O), 135.5, 132.5, 129.8, 127.7 (Ar-C_{24}), 113.7, 112.0, 110.4, 109.3 (sp^2-*C*), 64.8 (5, 6-*C*H_2O), 63.7 (5′, 6′-*C*H_2O), 48.3 (5-, 6-C), 40.7 (5′-, 6′-C) 26.7 (2 × C(*C*H_3)$_3$), 20.7 (2 × CO*C*H_3), 19.0 (2 × *C*(CH_3)$_3$); ν_{max} (thin film): 2955, 2922, 2856, 1749, 1721, 1462, 1428, 1380, 1273, 1224, 1114, 1073, 1034, 739, 701; *m*/*z* (AP): 1065 ([M]$^+$, 2), 893 (3), 565 (15), 383 (100); HRMS (EI): found: 1065.1469, $C_{50}H_{56}O_6S_8Si_2$ requires: 1065.1459.

***cis*,*trans*-Tetrakis(hydroxymethyl)-ET, 21.** A solution of **53** (0.23 g, 0.22 mmol) in a mixture of THF (20 ml) and 20% HCl solution (10 ml) was stirred under N_2 for 60 h. The solution was neutralised by the addition of solid $NaHCO_3$. The organic layer was collected, dried (Na_2SO_4) and evaporated to afford **21** (0.08 g, 73.3%) as an orange–brown solid; mp 154–155 °C; δ_H (MeOH-d_4): 3.83 (2H, m, 5′-, 6′-*H*), 3.64 (10H, m, 5-, 6-*H* & 5-, 6-, 5′, 6′-CH_2O); δ_C (MeOH-d_4): 113.1, 112.3, (sp^2-*C*), 65.0 (5-, 6-*C*H_2O), 63.0 (5′, 6′-*C*H_2O) 45.9 (5-, 5′-, 6-, 6′-*C*); ν_{max} (KBr): 3378, 2912, 2862, 1654, 1384, 1179, 1028; *m*/*z* (AP): 505 ([M + H]$^+$, 22); HRMS (EI): found: 503.8817, $C_{14}H_{16}O_4S_8$ requires: 503.8814.

Reaction of trithione 24 with alkene 54. A mixture of the diketal **54**[36] (0.50 g, 2.20 mmol) and the trithione **24** (0.86 g, 4.40 mmol) in toluene (25 ml) was refluxed for 8 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography (5 : 1 cyclohexane–ethyl acetate) to elute *5R,6R-5,6-bis((4′R)-2′,2′-dimethyl-1,3-dioxolan-4′-yl)-5,6-dihydro-1,3-dithiolo[4,5-b]1,4-dithiin-2-thione* **55** as a yellow solid (0.28 g, 30.0%), mp 164–165 °C; δ_H (400 MHz): 4.45 (2H, m, 2 × C*H*O), 4.18 (2H, dd, *J* = 9.1, 6.0, 2 × CH_αHO), 4.03 (2H, dd, *J* = 9.1, 4.2, 2 × CHH_βO), 3.71 (2H, d, *J* = 9.8, 5-, 6-*H*), 1.41 (6H, s, 2 × CH_3), 1.33 (6H, s, 2 × CH_3); δ_C (100 MHz): 206.5 (2-*C*), 118.9 (3a-, 7a-*C*), 110.6 (2 × 2′-*C*), 75.9 (2 × 4′-*C*), 67.8 (2 × 5′-*C*), 44.3 (5, 6-*C*), 27.1 (2 × *C*H_3), 25.3 (2 × *C*H_3); ν_{max} (KBr): 2988, 2935, 1488, 1458, 1377, 1368, 1235, 1148, 1066, 830; *m*/*z* (AP): 425 ([M + H]$^+$, 31), 177 (100); HRMS (ES): found: 425.0038 [M + H]$^+$, $C_{15}H_{20}O_4S_5$ + H requires: 425.0035; $[\alpha]_D^{25}$ = +489 (*c* = 0.12, DCM). Further elution with 1 : 1 cyclohexane–ethyl acetate gave a second fraction containing **56** and starting material **54** which was further purified by flash chromatography (dichloromethane) to give a yellow oil, which on trituration with ether gave *5S,6S-5,6-bis((4′R)-2′,2′-dimethyl-1,3-dioxolan-4′-yl)-5,6-dihydro-1,3-dithiolo[4,5-b]1,4-dithiin-2-thione* **56** as a yellow solid (0.05 g, 5.4%); mp 96–98 °C; δ_H: 4.42 (2H, m, 2 × C*H*O), 4.12 (2H, dd, *J* = 8.7, 6.4, 2 × CH_αHO), 3.86 (2H, dd, *J* = 8.7, 5.8, 2 × CHH_βO), 3.46 (2H, m, 5-, 6-*H*), 1.44 (6H, s, 2 × CH_3), 1.33 (6H, s, 2 × CH_3); δ_C: 208.8 (2-*C*), 128.3 (3a-, 7a-*C*), 110.3 (2 × 2′-*C*), 75.8 (2 × 4′-*C*), 66.9 (2 × 5′-*C*), 51.7 (5-,6-*C*), 26.4 (2 × *C*H_3), 25.0 (2 × *C*H_3); ν_{max} (KBr): 2990, 2929, 2877, 1464, 1380, 1269, 1212, 1154, 1052, 1024, 966, 920, 853, 514; $[\alpha]_D^{25}$ = −143 (*c* = 0.36, DCM); *m*/*z* (EI): 424 (M$^+$, 8), 101 (38), 84 (30), 76 (24), 72 (28), 49 (38), 43 (100); HRMS (ES): found 425.0041, $C_{15}H_{20}O_4S_5$ + H^+ requires: 425.0038.

Crystal data for ***56***. $C_{15}H_{20}O_4S_5$, M_r = 424.61, orthorhombic, *a* = 9.3614(7), *b* = 10.3321(4), *c* = 20.0889(15) Å, *V* = 1943.1(2) Å^3, *Z* = 4, $P2_12_12_1$, D_c = 1.45 g cm^{-3}, μ(MoKα) = 0.061 mm^{-1}, *T* = 120(2) K, 2508 unique reflections, 2239 with $F > 4\sigma(F)$, *R* = 0.061, *wR* = 0.098. The structure was solved and refined using the SHELXS and SHELXL computer packages.[44] CCDC reference number 230196. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b709823e

***5R,6R*-5,6-Bis((4′*R*)-2′,2′-dimethyl-1,3-dioxolan-4′-yl)-5,6-dihydro-1,3-dithiolo[4,5-*b*]-1,4-dithiin-2-one, 57.** To a solution of **55** (0.47 g, 1.10 mmol) in $CHCl_3$ (20 ml) and glacial acetic acid (6 ml) was added mercuric acetate (0.53 g, 1.65 mmol). After 2 h stirring at room temperature the mixture was filtered. The filtrate was washed consecutively with saturated $NaHCO_3$ solution (3 × 50 ml) and H_2O (50 ml), dried (Na_2SO_4) and evaporated to afford **57** as an orange solid (0.38 g, 84.0%); mp 116–118 °C; δ_H: 4.51 (2H, m, 2 × 4′-*H*), 4.20 (2H, dd, *J* = 8.9, 6.1, 2 × 5′-H_α), 4.04 (2H,

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dd, $J = 9.2$, 4.2, 2 × 5′-H_β), 3.71 (2H, d, $J = 9.9$, 5-, 6-H), 1.42 (6H, s, 2 × CH_3), 1.34 (6H, s, 2 × CH_3); δ_C: 188.9 (2-C), 110.6 (2 × 2′-C), 109.6 (3a-, 7a-C), 76.1 (2 × 4′-C), 68.0 (2 × 5′-C), 45.7 (5, 6-C), 27.1 (2 × CH$_3$), 25.4 (2 × CH$_3$); ν_{max} (KBr): 2988, 2935, 1683, 1381, 1372, 1260, 1245, 1229, 1214, 1074, 822; $[\alpha]_D^{25} = +206$ ($c = 0.14$, DCM); m/z (EI): 408 (100, M$^+$), 393 (15, [M − 15]$^+$); HRMS (EI): found 408.0190, $C_{15}H_{20}O_5S_4$ requires 408.0188.

***R*,*R*-*vic*-Bis((4″*R*)-2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)-ET, 58.** A mixture of oxo compound **57** (0.10 g, 0.25 mmol) and the thione **28** (0.08 g, 0.37 mmol) was heated in triethyl phosphite (5 ml) to 90 °C under N_2 for 5 h to give an orange solution. Triethyl phosphite was removed by distillation *in vacuo* and the residue purified by flash chromatography (3 : 1 cyclohexane–ethyl acetate) to yield **58** as an orange solid (0.05 g, 34.9%); mp 88–90 °C; δ_H: 4.37 (2H, m, 2 × 4″-H), 4.13 (2H, dd, $J = 9.1$, 5.9, 2 × 5″-H_α), 4.00 (2H, dd, $J = 9.1$, 4.4, 2 × 5″-H_β), 3.67 (2H, dd, $J = 8.9$, 1.0, 5-, 6-H), 3.26 (4H, s, 5′, 6′-H_2), 1.40 (6H, s, 2 × CH_3), 1.32 (6H, s, 2 × CH_3); δ_C: 113.9, 112.3, 110.4 (sp^2-C), 109.9 (2 × 2″-C), 76.5 (2 × 4″-C), 68.0 (2 × 5″-C), 44.9 (5, 6-C), 30.2 (5′, 6′-C), 27.1 (2 × CH$_3$), 25.4 (2 × CH$_3$); ν_{max} (KBr): 2978, 2916, 1654, 1650, 1638, 1618, 1560, 1510, 1456, 1384, 1368, 1249, 1213, 1145, 1062, 1016, 922, 834, 766, 507; $[\alpha]_D^{25} = +51.2$ ($c = 0.13$, DCM); m/z (EI): 584 (M$^+$, 2), 356 (5), 132 (9), 101 (14), 88 (23) 43 (100); HRMS (ES): found: 584.9507, $C_{20}H_{24}O_4S_8$ + H$^+$ requires: 584.9513; found C: 41.0, H: 4.0%, $C_{20}H_{24}O_4S_8$ requires C: 41.1, H: 4.1%.

***R*,*R*-*vic*-Bis((2″*R*)-1″,2″-dihydroxyethyl)-ET, 22.** Diketal **58** (60 mg, 0.12 mmol) was stirred with a mixture of aq. HCl (4 M, 4 ml) and THF (8 ml) under nitrogen for 12 h. Evaporation and drying *in vacuo* gave the tetrol **22** (49 mg, 94%) as a buff powder, mp 201–202 °C; δ_H (DMSO-d$_6$): 3.82 (2H, br d, $J = 9.5$, 5-, 6-H), 3.67 (2H, d, $J = 10.2$, 2 × CH_αH$_\beta$O), 3.60 (6H, m, 2 × CHCH$_\alpha$$H_\beta$O$H$), 3.34 (4H, s, 5′, 6′-$H_2$); δ_C (DMSO-d$_6$): 112.9, 110.5, 110.0, 109.9 (sp^2-C), 71.8 (2 × -CH(OH)), 63.3 (2 × -CH$_2$OH), 42.7 (5, 6-C), 29.5 (5′, 6′-C); ν_{max} (KBr): 3293, 2920, 1425, 1329, 1296, 1259, 1182, 1109, 1078, 1051, 1026, 958, 870, 818, 766, 626, 523; $[\alpha]_D^{25} = +69$ ($c = 0.035$, THF); m/z (EI): 504 (M$^+$, 1); HRMS (EI): found: 503.8818, $C_{14}H_{16}O_4S_8$ requires: 503.8809; found C: 33.3, H: 3.4%, $C_{14}H_{16}O_4S_8$ requires C: 33.3, H: 3.2%.

***R*,*R*,*R*,*R*-Tetrakis((4″*R*)-2″,2″-dimethyl-1″,3″-dioxolane-4″-yl)-ET, 59.** Oxo compound **57** (0.19 g, 0.46 mmol) was heated in triethyl phosphite (3 ml) to 90 °C under N_2 for 18 h to give an orange solution. Triethyl phosphite was removed by distillation *in vacuo* and the residue purified by flash chromatography (8 : 1 cyclohexane–ethyl acetate) to yield **59** as a pale orange solid (0.11 g, 60.2%); mp 176–178 °C (dec.); δ_H: 4.38 (4H, m, 4 × 4″-H), 4.18 (4H, dd, $J = 9.0$, 6.0, 4 × 5″-H_α), 4.03 (4H, dd, $J = 9.0$, 4.3, 4 × 5″-H_β), 3.70 (4H, dd, $J = 11.8$, 2.0, 5-,6-, 5′-,6′-H), 1.43 (12H, s, 4 × CH_3), 1.35 (12H, s, 4 × CH_3); δ_C: 111.0 & 109.9 (2-,2′-C & 3a-, 7a-, 3a′-, 7a′-C), 110.4 (4 × 2″-C), 76.0 (4 × 4″-C), 68.0 (4 × 5″-C), 44.9 (5-, 6-, 5′-, 6′-C), 27.1 (4 × CH$_3$), 25.4 (4 × CH$_3$); ν_{max} (KBr): 2986, 2933, 2880, 1458, 1382, 1371, 1248, 1215, 1150, 1065, 970, 923, 836, 774, 513; $[\alpha]_D^{25} = +65.3$ ($c = 0.15$, DCM); m/z (APCI): 785 ([M + 1]$^+$, 25), 727 (24), 569 (100), 73 (58); HRMS (EI): found: 784.0485, $C_{30}H_{40}O_8S_8$ requires: 784.0483; found C: 46.0, H: 5.1%, $C_{30}H_{40}O_8S_8$ requires C: 45.9, H: 5.1%.

***R*,*R*,*R*,*R*-Tetrakis((2″*R*)-1″,2″-dihydroxyethyl)-ET, 23.** Tetraketal **33** (40 mg, 0.051 mmol) was stirred with a mixture of aq. HCl (4 M, 1.5 ml) and THF (11 ml) under nitrogen for 24 h. Evaporation and drying *in vacuo* gave the tetrol **23** (26 mg, 82%) as a brown–buff powder, mp >330 °C (some contraction at 170–172 °C). δ_H (400 MHz, DMSO-d$_6$ + one drop D$_2$O): 3.61 (16H, m, 4 × SCH-CH(OH)-CH_2OH); δ_C (100 MHz, DMSO-d$_6$): 110.5 & 109.8 (3a-, 3a′-, 7a-, 7a′-C & 2′,2′-C), 71.8 (4 × -CH(OH)), 63.3 (4 × -CH$_2$OH), 42.7 (5-, 5-′, 6-, 6′-C); ν_{max} (KBr): 3254 br, 2962, 1404, 1259, 1082, 1013, 869, 792, 700, 676, 661; $[\alpha]_D^{25} = +187.5$ ($c = 0.048$ in DMF); m/z (ES$^+$): 647 ([M + Na], 3), 279 (20), 171 (23), 47 (100); m/z (ES$^-$) 659 ([M + CH$_3$OH], 4), 623 ([M − H], 6), 475 (5), 311 (8), 228 (14), 227 (15), (226, 14), 179 (12), 127 (5), 69 (100); HRMS (ES$^+$): found: 624.9315, $C_{18}H_{24}O_8S_8$ + H requires: 624.9310; found C: 34.5, H: 4.1%, $C_{18}H_{24}O_8S_8$ requires C: 34.6, H: 3.9%.

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