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CHIRAL THIOPHENE DIOXIDES AND THIOPHENE S,N-YLIDES AS DIENES FOR ASYMMETRIC DIELS-ALDER APPLICATION

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Dedicated to the most youthful enthusiast I have had the pleasure to meet, Ted Taylor, on his 65th birthday

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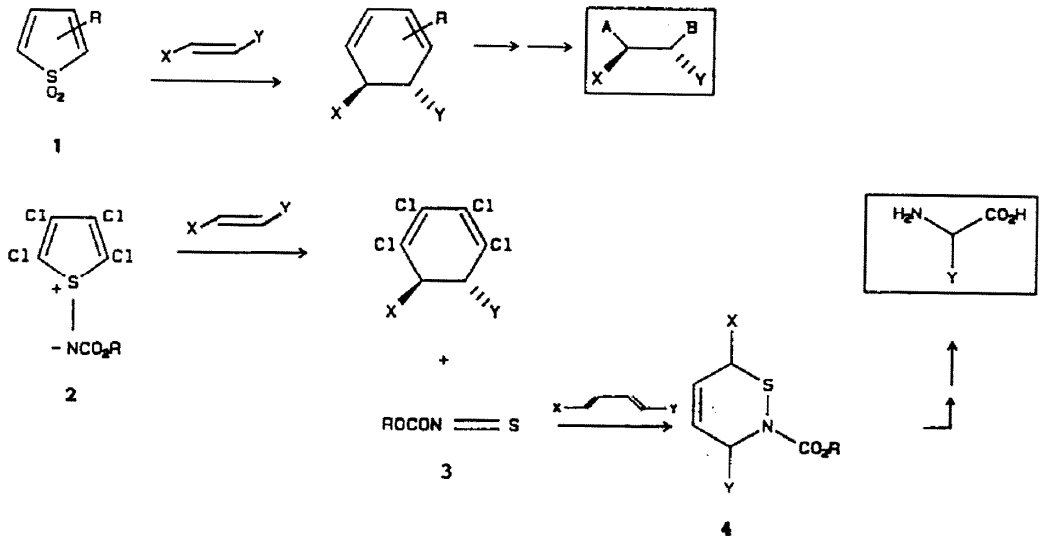
Abstract: 2-Menthyltrihalothiophene S,S-dioxides are efficient asymmetric dienes in Diels-Alder reactions with dienophiles to give regio- and stereoisomerically pure adducts. Thus styrene, allyl alcohol, methyl acrylate and acrylamide give solely one adduct while flat dienophiles such as indene and acenaphthylene give two diastereomers. Analogous 1- and 3- chirally substituted thiophenes are of little value in generating pure single adducts. Further transformations of the above adducts into useful enantiomerically pure compounds is briefly discussed.

Introduction

The tremendous growth and versatility of asymmetric Diels-Alder reactions in synthesis has largely been developed utilising a chirally substituted dienophile to induce stereocontrol.[1] Relatively few easily accessible and generally useful chiral dienes have been employed.[2] The remarkable diene reactivity of tetrachlorothiophene dioxide (1, R = Cl_4) with both electron-rich and electron-poor



Scheme 1

dienophiles,[3] coupled with the complementary reactivity of the analogous ylides[4] 2 led us to consider them as potential asymmetric inductors in Diels-Alder applications (Scheme 1). There are three sites of attachment of an asymmetric substituent to a thiophene ring; the 1-, 2-, or 3-position.

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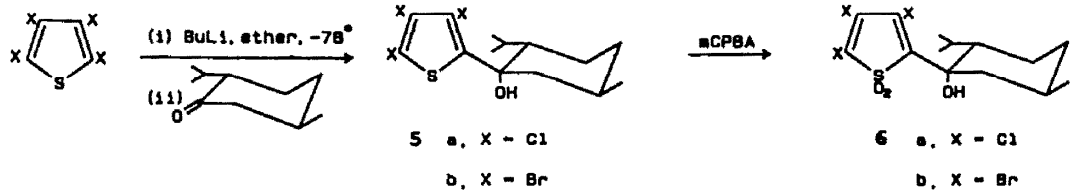
The synthesis of chiral 2- and 3-substituted thiophene dioxides

Tetrachlorothiophene is readily transformed into α-substituted derivatives via the α-lithio compound[5] (Scheme 2). In this way using menthone, the menthol



5 a, X = Cl
b, X = Br

6 a, X = Cl
b, X = Br

Scheme 2

derivative 5 was produced in 87% yield. Subsequent oxidation with m-chloroperbenzoic acid gave the corresponding dioxide 6a in 96% yield as a colourless crystalline product. In a similar way the tribromothienylmenthol 6b dioxide was prepared with stepwise yields of 60 and 63% respectively.

X-ray crystallographic examination of the menthol derivative 6a confirmed both the structure and axial geometry of the OH-group and revealed a useful weak hydrogen bond between the OH-group and one of the oxygens of the sulphone function (Figure 1). This effectively locks the menthol unit so as to protect the back face of the thiophene from attack. The X-ray crystallographic details are given in Table 1 (see experimental section).

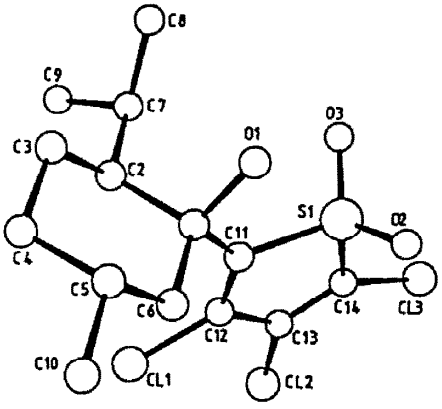
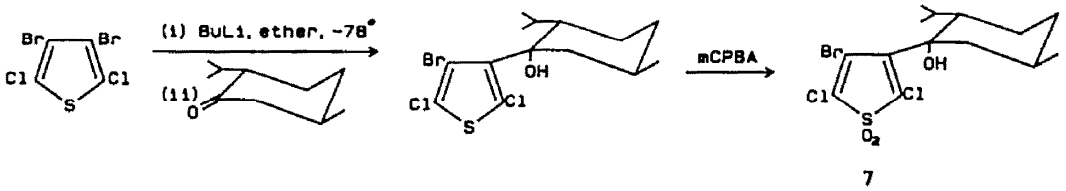


Figure 1

The syntnesis of the analogous 3-menthylthiophene dioxide required a related approach utilising 2,5-dichloro-3,4-dibromothiophene (Scheme 3). In this way the



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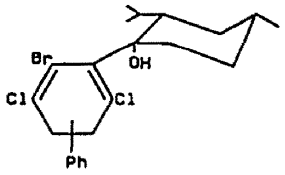
Scheme 3

dioxide 7 was synthesised in an overall 20% yield.

Cycloadditions to the 2- and 3-menthylthiophene dioxides

The thienylmenthol dioxides 6 and 7 underwent ready cycloadditions with electron-rich dienophiles and slowly with some electron-poor dienophiles. The 3-substituted derivative 7 showed little regio- or diastereo-discrimination in its cycloaddition to styrene, all four inseparable isomers 8 being produced in a total 90% yield at ambient temperature. Its interaction with acenaphthylene was of interest in that reaction was complete in 3 h in refluxing toluene solution but required 8 days in methylene chloride. Surprisingly, the product 9 was obtained apparently as one pure isomer (indicated by t.l.c.) in 87% yield. The bridging aliphatic protons appeared as a broad singlet unchanged by addition of a chiral shift reagent. However, closer examination of the product by ^{13}C n.m.r. clearly indicated 9 to be a mixture of diastereoisomers in a ratio of about 4.7:1.



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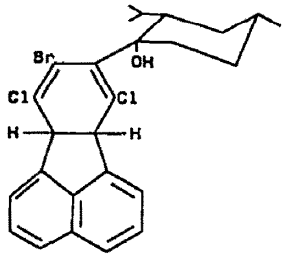

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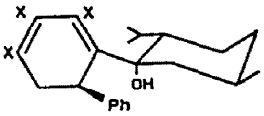
By contrast the 2-menthylthiophene dioxide 6a reacted with styrene somewhat slower than the 3-menthyl analogue 7 but with complete diastereo- and regiospecificity. After 2 days in refluxing ethanol the pure adduct 10a was obtained in 95% yield. Less polar solvents (e.g. refluxing toluene) proved less effective, the cycloaddition being incomplete after 5 days. The structure and regiochemistry was confirmed by spectroscopic means (see experimental) and by X-ray crystallography which gave less than ideal data due to the destruction of the crystal by the X-ray bombardment (Figure 2). The limited data is recorded in Table 1. The regiochemistry is that predicted by application of simple frontier orbital theory.[6] The corresponding tribromothienyl menthol 6b reacted similarly (2 d, refluxing n-butanol, 85% yield) to give the isomerically pure adduct 10b.



10 a, X = Cl

b, X = Br

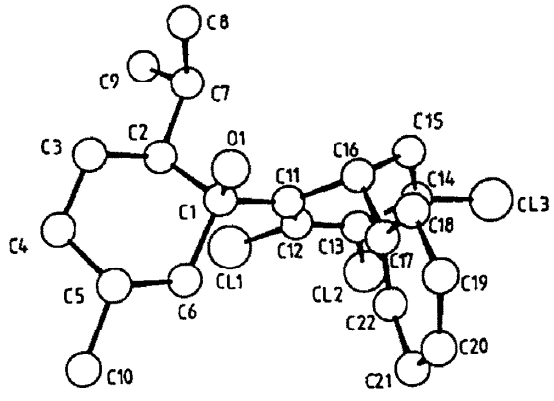
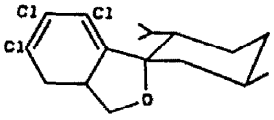


Figure 2

Allyl alcohol underwent a slow cycloaddition (neat under reflux, 3 days, 62% yield) to give a product by loss of water from the initial adduct, to which we assign the ether structure 11. Although all the analytical data supports this structure, the ^{1}H n.m.r. spectroscopy is, at first sight, rather puzzling. The

five allyl alcohol-derived protons show a remarkably complex coupling pattern even at 500 MHz, in which each proton is non-equivalent and couples to all the other four protons. A ^1H-^1H-COSY experiment clearly identified this group of protons while a HETCOR study gave unequivocal support for the CH_2CHCH_2O unit. Once again, only one regio- and diastereoisomer was isolated.



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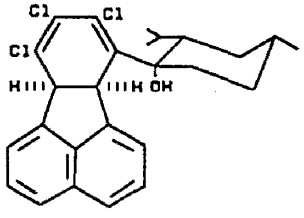
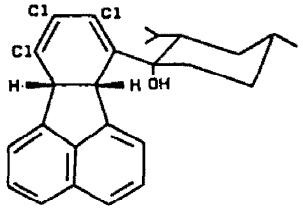
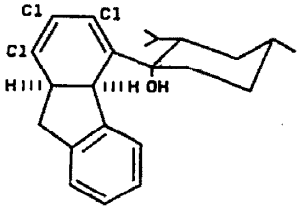


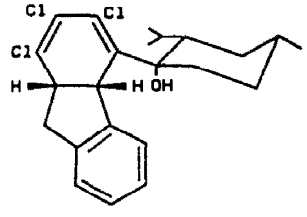
12a



12b



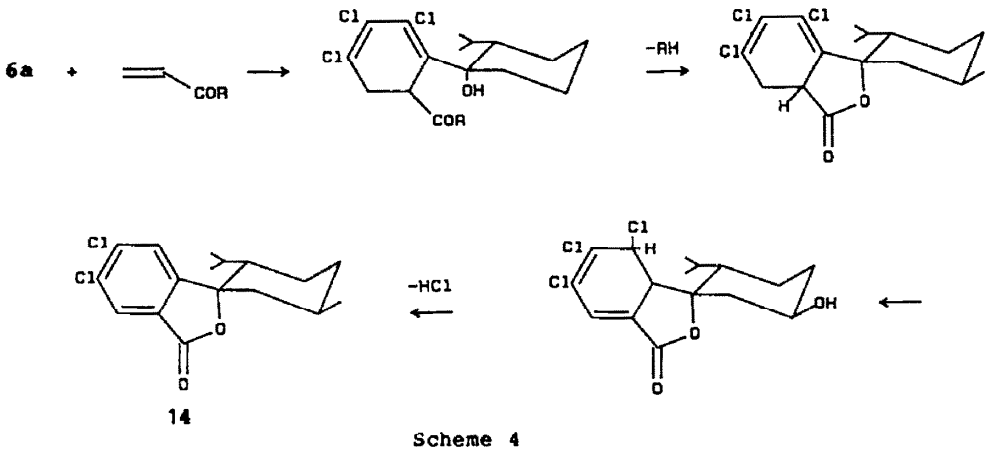
13a



13b

The use of flat nucleophilic dienophiles such as acenaphthylene and indene proved remarkably unreactive and non-stereospecific. Acenaphthylene was surprisingly slow to react with 6a, the reactants being largely unchanged after 7 days refluxing in toluene. However, after refluxing in n-butanol for 3 days, the diastereoisomeric adducts 12a and 12b were isolated (75% yield) in a ratio of 77:23. Indene reacted somewhat faster with 6a, the reactants being consumed in 24 h in refluxing n-butanol. The diastereoisomeric adducts 13a and 13b were obtained in a ratio of 93:7 in 86% yield. Despite attempted difference n.O.e. studies of the adducts 13, we were unable to define the structure of the diastereomers 13a and 13b unambiguously. The major isomers of both acenaphthylene and indene adducts showed remarkably similar n.m.r. characteristics in respect of the aliphatic menthyl protons, as was the case with the minor isomers. This suggests that the structures of the major adducts 12 and 13 are related as are those of the minor adducts.

Use of electron-deficient ethylenes was only partially effective. Thus while methyl vinyl ketone, acrylonitrile, N-vinyl-2-pyrrolidone and phenyl vinyl sulphone showed little inclination to react with the thiophene dioxide 6a, methyl acrylate and acrylamide both reacted slowly (ester: neat under reflux, 3 days, 69%; amide: ethanol solution, 7 days, 61%) to give the aromatised lactone (14, Scheme 4) in both cases. Again, a secondary cyclisation occurred subsequent to cycloaddition. No regio- or stereoisomers were observed in these cases.

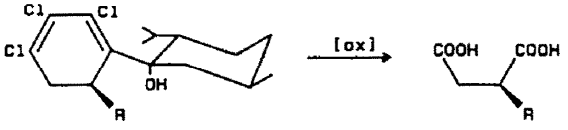


Scheme 4

We have noted elsewhere that 1-substituted derivatives such as the ylides 2 undergo ready cycloaddition. The extruded unit, a thionitroso compound 3 is also a potentially valuable chiral dienophile capable of being trapped by dienes or by alkenes in an ene reaction.[4] However, the 1-substituted systems have the chiral substituent distant from the cycloaddition site and offered little prospect of regioselective addition to the symmetrical thiophene ring. This was borne out in practice. Trapping of the thionitroso compound 3 from the ylides (2; R,a = (-)-menthyl, b = (+)fenchyl) gave thiazines (e.g. 4) with no diastereodifferentiation (the adducts obtained as inseparable mixtures of diastereoisomers). Unfortunately, we nave so far been unable to generate the corresponding ylides bearing the well established chiral auxiliaries described by Corey[7] and Oppolzer.[8]

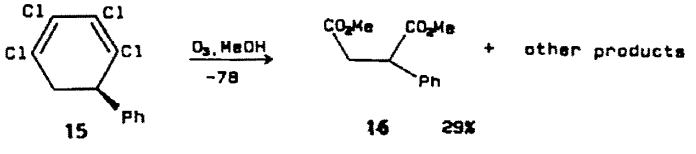
Transformations of the Cycloadducts

Having a family of adducts readily available, we next explored the prospect for useful transformation of the adducts into simple enantiomerically pure



Scheme 5

compounds (e.g. Scheme 5). As a model compound we first examined the racemic styrene adduct of tetrachlorothiophene dioxide[3] 15. Ozonation proved very slow and inefficient (presumably due to the well-known difficulties of ozonation of C-C olefinic systems bearing chlorine atoms[9] and also to competing ozonolysis of the phenyl substituent). However methyl phenylsuccinate 16 was isolated in low yield.



Oxidation with permanganate and sodium periodate was totally ineffective. Attempts to remove the problematic chlorine atoms first were next examined. Tributyltin

hydride[10] under photolysis gave solely starting material, whereas ammonium formate, known as a powerful transfer-hydrogenolysis reagent in the presence of palladium[11] gave a mixture of biphenyl, 1-phenylcyclohexene and phenyl cyclohexane!

Oxidation of the styrene adduct of trichlorothienylmenthol **10a** was next explored. Ozonolysis in carbon tetrachloride, methanol or methylene chloride gave complex mixtures with no evidence of phenylsuccinic acid derivatives (e.g. **16**) being present, even after subsequent further oxidation of the mixtures.

Potassium permanganate in benzene containing 18-crown-6 ('purple benzene')[12] was totally without effect. Vanadium catalysed nitric acid oxidation[13] gave numerous products with no evidence of phenylsuccinic acid derivatives. Transfer hydrogenolysis also yielded a mixture of dechlorinated products.

In conclusion, the principle of efficient chiral induction in cycloadditions to halothiophene dioxides bearing an asymmetric 2-substituent has been established. The requirement for an easily cleaved chiral auxilliary remains and is now under active exploration.

Experimental

M.p.s were recorded on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were obtained on Perkin-Elmer 257 or 883 spectrophotometers and ^1H n.m.r. spectra on a Varian EM-390 or Bruker WM 500 spectrometer operating at 90 or 500 MHz respectively. The n.m.r. data refer to deuteriochloroform solutions relative to tetramethylsilane as internal standard. ^{13}C N.m.r. (125 MHz) spectra were recorded on the Bruker WM 500 spectrometer for deuteriochloroform solutions. Mass spectra were taken on a Varian MAT 212 instrument. Chromatography used silica throughout; t.l.c. plates were Merck Silica Gel 60 F254, while for column chromatography Merck Silica Gel 60 (70-230 mesh) was used. Flash chromatography utilized Merck Silica Gel 60 (230-400 mesh). Petrol refers to light petroleum, b.p. 60-80°C.

1-(3,4,5-Trichlorothien-2-yl)-(1R,2S,5R)-menthol 5a

To a solution of tetrachlorothiophene (11.1 g, 0.05 mmol) in dry ether (100 ml) at -78° under an atmosphere of N_2, n-butyl lithium (1.6 M solution, 35 ml, 0.056 mol) was added. A suspension was formed which was stirred at -78° for 30 min and a solution of (-)-menthone (7.70 g, 0.05 mol) in dry ether (25 ml) was then added. The resulting solution was allowed to attain room temperature and stirred for a further 1 h, poured into water and the ether layer separated, dried ($MgSO_4$) and evaporated. Chromatography on silica (light petroleum) gave the title compound as a white solid which recrystallised from pentane as water-white needles (14.8 g, 87%), m.p. 69.5-71°C (Found: C, 49.2; H, 5.54. $C_{14}H_{19}Cl_3OS$ requires C, 49.2; H, 5.60%); ν_{max} (Nujol) 3600 (OH) cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.80-0.95 (9H, m, CH_3's), 1.3-2.0 (9H, m, aliphatics), 2.30 (1H, bs, OH); m/z 340 (M^+), 305, 255, 228, 165, 110.

1-(3,4,5-Tribromothien-2-yl)-1R,2S,5R)-menthol 5b

In a similar manner, tetrabromothiophene gave the title compound as a white solid (60%). Recrystallisation of a sample from petrol yielded water-white needles, m.p. 103-104°C (Found: C, 35.5; H, 4.12. $C_{14}H_{19}Br_3SO$ requires C, 35.4; H, 4.03%); ν_{max} (Nujol) 3600 (OH) cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.80-1.00 (9H, m, CH_3's), 1.15-2.1 (9H, m, aliphatics), 2.40 (1H, bs, OH).

1-(3,4,5-Trichlorothien-2-yl)-(1R,2S,5R)-menthol S,S dioxide 6a

To a solution of MCPBA (85%, 8.50 g, 0.042 mol) dissolved in warm 1,2-dichloroethane (50 ml) was added 5a (5.00 g, 0.015 mol). The solution was refluxed for 3 h, allowed to cool and 3-chlorobenzoic acid was filtered off. The cake was washed with cold 1,2-dichloroethane (10 ml) and the combined filtrates were washed with aqueous sodium carbonate (10%) until free of acid. The filtrate was dried ($MgSO_4$) and evaporated to give 6a as a white solid. Recrystallisation from methanol afforded water-white needles (5.30 g, 96%), m.p. 122.5–123.5°C (Found: C, 45.1; H, 5.20. $C_{14}H_{19}Cl_3SO_3$ requires C, 45.0; h, 5.10%); ν_{max} (Nujol) 3600 (OH), 1320 and 1160 (SO_2) cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.90–1.03 (9H, m, CH_3's), 1.50–2.10 (10H, m, aliphatics and OH).

1-(3,4,5-Triboromothien-2-yl)-(1R,2S,5R)-menthol S,S dioxide 6b

In a similar manner, treatment of tribromothienyl menthol with MCPBA gave the dioxide 6b as a white solid. Recrystallisation from petrol afforded water-white prisms (63%), m.p. 185–187°C (Found: C, 33.6; H, 3.63. $C_{14}H_{19}Br_3SO_3$ requires C, 33.2; H, 3.78%); ν_{max} (Nujol) 3600 (OH), 1300 and 1150 (SO_2) cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.70–0.90 (9H, m, CH_3's), 1.15–2.20 (9H, m, aliphatics), 2.38 (1H, bs, OH).

1-(4-Bromo-2,5-dichlorothien-3-yl)-(1R,2S,5R)-menthol S,S-dioxide 7

To a solution of 3,4-dibromo-2,5-dichlorothiophene[14] (5.00 g, 16 mmol) in dry ether (50 ml) at -78°C, n-butyl lithium (1.6 M solution, 11.3 ml, 18.8 mmol) was added dropwise and the resulting solution stirred for 15 min. Then a solution of (-)-menthone (2.48 g, 16 mmol) in dry ether (20 ml) was added. The resulting solution was allowed to attain room temperature and stirred for a further 1 h, poured into water and the ether layer separated, dried ($MgSO_4$) and evaporated. Chromatography of the residual oil (petrol:CH_2Cl_2, 1:1, as eluant) gave the title compound as a colourless oil (2.32 g, 37%); ν_{max} 3590 (OH) cm^{-1}; δ_H (90 MHz, $CDCl_3$), 0.80–1.05 (9H, m, CH_3's), 1.10–2.60 (10H, m, aliphatics and OH).

A solution of the thienyl menthol (1.00 g, 2.6 mmol) and MCPBA (85%, 1.30 g, 6.5 mmol) in 1,2-dichloroethane (10 ml) was refluxed for 2 h. The solution was cooled and 3-chlorobenzoic acid filtered off. The cake was washed with cold 1,2-dichloro- ethane (5 ml) and then the combined extracts were evaporated to give a slightly discoloured oil. Chromatography (petrol:ethyl acetate, 10:1, as eluant) gave a white solid. Recrystallisation from ethyl acetate-petrol gave 7 as white plates (0.60 g, 54%), m.p. 126.5–127.5°C (Found: C, 40.0; H, 4.54. $C_{14}H_{19}BrCl_2SO_3$ requires C, 40.2; H, 4.54%); ν_{max} (Nujol) 3540 (OH), 1330 and 1165 (SO_2) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.83–0.90 (9H, m, CH_3's), 1.15–2.35 (9H, m, aliphatics), 2.50 (1H, bs, OH).

Preparation of Thiophene S.N-Ylides

(1) Preparation of Menthyl azidoformate

To a solution of (-)-menthol (20.0 g, 0.13 mol) in dry pyridine (20 ml) cooled in an ice-bath, phenyl chloroformate (17.7 ml, 0.14 mol) was added slowly with vigorous stirring. A white precipitate formed. The mixture was stirred at room temperature overnight and was then poured into water and the mixture extracted with ether. The ethereal extract was then washed successively with aqueous citric acid (10%), aqueous sodium hydrogen carbonate and finally water. The extract was dried ($MgSO_4$) and evaporated to give menthyl phenyl carbonate as a colourless oil (32.0 g, 95%), ν_{max} (liquid film) 1750 (CO) and 1230 (C-O-C) cm^{-1}; δ_H (90 MHz, $CDCl_3$)

0.80-1.00 (9H, m, CH_3's), 1.03-2.25 (9H, m, aliphatics), 4.60 (1H, dt, J 11 Hz, CH), 7.10-7.45 (5H, m, aromatics).

To a solution of menthyl phenyl carbonate (32.0 g, 0.12 mol) in ethanol (75 ml) was added hydrazine hydrate (25 ml, 0.42 mol). The solution was refluxed for 1 h and allowed to cool. The solution was poured into water and extracted with ether. The extract was washed successively with aqueous sodium hydroxide (10%) and water, dried ($MgSO_4$), and evaporated to give menthyl carbazate as a white solid (24.5 g, 95%), ν_{max} (Nujol) 3400 (NH) and 1630 (CO) cm^{-1}. The crude carbazate was used without purification.

The crude menthyl carbazate (24.5 g, 0.11 mol) was dissolved in acetic acid (30 ml) and the solution cooled below 5°C, stirred and treated dropwise with a solution of sodium nitrite (9.00 g, 0.13 mol) in water (20 ml). The temperature was maintained below 5°C. On addition of the aqueous sodium nitrite, a precipitate formed. After the addition was complete, the mixture was stirred for a further 15 min below 5°C and then for 1 h at room temperature. The resulting mixture was then poured into water and extracted with ether. The extract was washed successively with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$) and evaporated *in vacuo*. Chromatography of the residual oil (CH_2Cl_2 as eluant) gave a yellow oil which solidified on standing. Recrystallisation from petrol afforded (-)-menthyl azidoformate as white needles (20.0 g, 78%), m.p. 30-30.5°C (lit., m.p. 28-30°C).[15]

In a similar manner, (+)-fenchyl azidoformate was prepared as water-white plates (from methanol), m.p. 45-46°C (Found: C, 59.2; H, 7.77; N, 18.7. $C_{11}H_{17}N_3O_2$ requires C, 59.2; H, 7.67; N, 18.8%); ν_{max} (Nujol) 2190, 2130 (N_3), 1725 (CO) and 1245 (C-O-C) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.83 (3H, s, CH_3), 1.06 (3H, s, CH_3), 1.09 (3H, s, CH_3), 1.19-1.86 (7H, m, aliphatics), 4.35 (1H, d, J 1.8 Hz, CH).

(2) Preparation of Thiophene S,N-Ylides 2

(-)-Menthyl azidoformate (13.0 g, 0.057 mol) was added dropwise to tetrachlorothiophene (80.0 g, 0.36 mol) at 135°C. The solution was stirred until no more nitrogen evolved (1 h), and the excess of tetrachlorothiophene was distilled off under reduced pressure. The residue was then chromatographed (CH_2Cl_2 as eluant) to give a red oil. Crystallisation from hexane afforded N-(-)-menthoxycarbonyl(2,3,4,5-tetrachloro-1-thiophenio)amide, **2a** (7.00 g, 29%) as white needles, m.p. 97-98°C (Found: C, 43.2; H, 4.63; N, 3.36. $C_{15}H_{19}Cl_4NO_2S$ requires C, 43.0; H, 4.57; N, 3.34%); ν_{max} (Nujol) 1670 (CO) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.80-2.30 (18H, m, aliphatics), 4.55 (1H, dt, J 11.0 and 5.0 Hz, CH).

Similarly, decomposition of (+)-fenchyl azidoformate in tetrachlorothiophene gave after crystallisation, N-(+)-fenchoxycarbonyl-(2,3,4,5-tetrachloro-1-thiophenio)amide, **2b** (48%) as water-white plates, m.p. 135-137°C (from methanol) (Found: C, 43.1; H, 4.18; N, 3.44. $C_{15}H_{17}Cl_4NO_2S$ requires C, 43.2; H, 4.11; N, 3.36%); ν_{max} (Nujol) 1660 (CO) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.83 (3H, s, CH_3), 1.00-1.90 (7H, m, aliphatics), 1.10 (6H, s, CH_3's), 4.30 (1H, d, J 1.8 Hz, CH).

Reaction of 6 with Styrene

A solution of **6a** (0.72 g, 1.93 mmol) and styrene (0.21 g, 2.02 mmol) in ethanol (2 ml) was refluxed for 2 days. The solution was concentrated *in vacuo* and chromatographed (petrol:ethyl acetate, 100:1) to give a colourless oil which solidified on standing. Recrystallisation from pentane gave the adduct **10a** (0.76

g, 95%) as white plates, m.p. 60–62°C (Found: C, 63.6; H, 6.55. $C_{22}H_{27}Cl_3O$ requires C, 63.8; H, 6.57%); δ_H (90 MHz, $CDCl_3$) 0.75–1.00 (9H, m, CH_3's), 1.00–2.65 (10H, m, aliphatics and OH), 2.55 (1H, dd, J 17 and 0.7 Hz, C<u>H</u>$_2$), 3.35 (1H, dd, J 17 and 8.5 Hz, C<u>H</u>$_2$), 4.40 (1H, dd, J 8.5 and 0.7 Hz, CH), 7.30 (5H, bs, aromatics).

Similarly, a solution of styrene (1.37 g, 13.2 mmol) and **6b** (3.00 g, 7.50 mmol) in <u>n</u>-butanol (5 ml) was refluxed for 24 h. After concentration of the solution <u>in vacuo</u>, the resulting oil was chromatographed (petrol) to give a colourless oil. Crystallisation from methanol afforded **10b** as a white crystalline solid (2.70 g, 85%), m.p. 64–66°C (Found: C, 47.8; H, 4.90. $C_{22}H_{27}Br_3O$ requires C, 48.2; H, 4.97%); δ_H (90 MHz; $CDCl_3$) 0.70–2.65 (19H, m, aliphatics and OH), 2.60 (1H, dd, J 16.5 and 0.7 Hz, C<u>H</u>$_2$), 3.25 (1H, dd, J 16.5 and 7.5 Hz, C<u>H</u>$_2$), 4.30 (1H, dd, J 7.5 and 0.7 Hz, CH), 7.25 (5H, bs, aromatics).

Reaction of 6a with methyl acrylate

A solution of **6a** (1.00 g, 2.68 mmol) in methyl acrylate (10 ml) was refluxed for 3 days. Concentration of the resulting solution <u>in vacuo</u> followed by chromatography (petrol:ethyl acetate, 50:1) gave a white solid. Recrystallisation from petrol gave the lactone **14** as white needles (0.60 g, 69%), m.p. 149–152°C (Found: C, 62.6; H, 6.19. $C_{17}H_{20}Cl_2O_2$ requires C, 62.4; H, 6.16%); ν_{max} ($CHCl_3$) 1760 (CO) and 1215 (C–O–C) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.70–2.10 (18H, aliphatics), 7.45 (1H, s, aromatic CH), 7.93 (1H, s, aromatic CH); δ_C (500 MHz; $CDCl_3$) 167.8 s, 153.2 s, 139.0 s, 133.6 s, 127.3 d, 126.1 s, 123.0 d, 90.8 s, 48.6 d, 47.3 t, 34.4 t, 28.9 d, 26.7 d, 23.3 t, 21.8 q, 21.7 q, 17.8 q.

Reaction of 6a with acrylamide

A solution of **6a** (1.00 g, 2.68 mmol) and acrylamide (0.95 g, 13.4 mmol) in ethanol (10 ml) was refluxed for 7 days. Concentration of the resulting solution followed by flash chromatography (petrol:ether, 95:5) gave the lactone **14** (0.37 g, 61% based on starting material consumed) identical in all respects to that formed from methyl acrylate, together with some unreacted **6a** (0.30 g).

Reaction of 7 with acenaphthylene

A solution of the dioxide **7** (0.15 g, 0.36 mmol) and acenaphthylene (0.06 g, 0.39 mmol) in toluene (2 ml) was refluxed for 3 h. Concentration of the resulting brown solution followed by flash chromatography (hexane as eluant) gave a white solid which upon recrystallisation from hexane afforded **9** as water-white plates (0.16 g, 87%), m.p. 169–170.5°C (Found: C, 61.0; H, 5.30. $C_{26}H_{27}BrCl_2O$ requires C, 61.6; H, 5.38%); ν_{max} ($CHCl_3$) 3600 cm^{-1} (OH); δ_H (90 MHz; $CDCl_3$) 0.75–2.40 (19H, aliphatic menthyl protons and OH), 4.55 (2H, s, bridging CH's), 7.40–7.80 (6H, m, aromatics); m/z, 506 (M^+), 470, 389, 353, 304, 236, 200, 153, 109, 69 (100) 41.

Reaction of 6a with allyl alcohol

A solution of **6a** (1.00 g, 2.8 mmol) in allyl alcohol (5 ml) was refluxed for 3 days. The solution was concentrated <u>in vacuo</u>. Flash chromatography (hexane) gave the adduct **11** as a white solid (0.60 g; 62%) which recrystallised from hexane as white needles, m.p. 182–183.5°C (Found: C, 58.6; H, 6.48. $C_{17}H_{23}Cl_3O$ requires C, 58.7; H, 6.23%); ν_{max} ($CHCl_3$) 1210 (C–O–C) cm^{-1}; δ_H (500 MHz; $CDCl_3$) 0.85–0.96 (9H, m, CH_3's), 1.48–1.53 (5H, m, aliphatics), 1.73 (2H, m, aliphatic CH_2), 1.86 (1H, m, aliphatic CH), 2.12 (1H, dd, aliphatic CH), 2.56 (2H, m, CH_2), 3.48 (2H, m,

CH and OCH_2), 4.14 (1H, m, OCH_2); δ_C (500 MHz; $CDCl_3$) 144.2 s, 128.6 s, 116.7 s, 90.93 s, 71.6 t, 45.6 d, 44.9 t, 42.6 d, 34.8 t, 34.6 t, 28.3 d, 28.1 d, 23.7 t, 22.1 q, 21.6 q, 17.9 q.

Reaction of 6a with acenaphthylene

Reflux a solution of **6a** (113 mg, 0.30 mmol) and acenapthylene (55 mg; 0.36 mmol) in n-butanol (2 ml) for 3 days. The solution was concentrated *in vacuo* and chromatographed (petrol) to give firstly **12a** as a colourless oil which solidifies on standing (81 mg, 58%); ν_{max} ($CHCl_3$) 3630 (OH) cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.80-2.61 (19H, m, menthyl protons and OH), 4.50 (1H, d, J 9.0 Hz, CH), 5.10 (1H, d, J 9.0 Hz, CH), 7.35-7.75 (6H, m, aromatics); δ_C (500 MHz, $CDCl_3$) 144.4 s, 141.4 s, 141.2 s, 136.4 s, 132.5 s, 130.4 s, 127.4 d, 126.9 d, 123.6 d, 123.2 d, 123.1 d, 120.2 d, 80.1 s, 49.5 d, 48.5 d, 45.7 d, 43.2 5, 34.4 t, 28.5 d, 28.3 d, 24.0 t, 22.3 q, 21.0 q, 18.7 q; m/z 460 (M^+), 407, 371., 339, 283, 236, 200, 152, 94, 69, 41, followed by its diastereoisomer **12b** as a white solid (24 mg, 17%) which gave upon recrystallisation from ethyl acetate-hexane water-white prisms, m.p. 216-218°C (Found: C, 68.0; H, 5.94; Cl, 23.0. $C_{26}H_{27}Cl_{30}$ requires C, 67.6, H, 5.89; Cl, 23.0%); ν_{max} ($CHCl_3$) 3630 (OH) cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.90-3.00 (19H, m, menthyl protons and OH), 4.45 (1H, d, J 8.5 Hz), 4.95 (1H, d J 8.5 Hz), 7.45-7.80 (6H, m, aromatics); δ_C (500 MHz; $CDCl_3$) 144.0 s, 141.0 s, 136.5 s, 132.8 s, 130.2 s, 127.5 d, 126.7 d, 123.7 d, 123.0 d, 123.0 d, 120.7 d, 82.0 s, 50.8 d, 47.8 d, 46.4 t, 45.9 d, 34.8 t, 28.6 d, 28.1 d, 23.9 t, 22.4 q, 22.1 q, 19.8 q; m/z 460 (M^+), 425, 389, 339, 270, 236, 200, 152, 95, 69, 41.

Reaction of 6a with indene

A solution of **6a** (1.00 g, 2.80 mmol) and indene (0.35 ml, 3.00 mmol) in n-butanol (5 ml) was refluxed for 24 h. Concentration of the resulting solution *in vacuo* followed by flash chromatography (petrol:ether, 20:1) gave firstly the adduct **13a** which gave upon recrystallisation from hexane water-white needles (0.95 g, 80%), m.p. 175-176.5°C (Found: C, 64.8, H, 6.32. $C_{23}H_{27}Cl_3O$ required C, 64.9; H, 6.39%); ν_{max} ($CHCl_3$) 3600 (OH) cm^{-1}; δ_H (500 MHz; $CDCl_2$) 0.98-2.73 (19H, aliphatics and OH), 3.24 (1H, dd, J 15.6 and 6.3 Hz, CH_2), 3.54 (1H, dd, J 7.3 and 6.3 Hz, CH), 3.63 (1H, d, J 15.6 Hz, CH_2), 4.68 (1H, d, J 7.3 Hz, CH), 7.22-7.28 (4H, m, aromatics); δ_C (500 MHz; $CDCl_3$) 142.7 s, 142.5 s, 140.3 s, 134.5 s, 127.7 s, 127.2 d, 126.6 d, 123.6 d, 123.4 d, 121.2 s, 79.9 s, 47.9 d, 46.6 d, 45.7 d, 43.5 t, 37.6 t, 34.4 t, 28.6 d, 28.3 d, 23.9 t, 22.3 q, 20.7 q, 18.5 q, followed by its diastereoisomer **13b** as a white solid. Recrystallisation from hexane afforded white needles (0.07 g, 6%), m.p. 173-174°C (Found: C, 65.0; H, 6,35. $C_{23}H_{27}Cl_3O$ required C, 64.9; H, 6.39%); ν_{max} ($CHCl_3$) 3600 (OH) cm^{-1}; δ_H (500 MHz; $CDCl_3$) 0.98-2.92 (19H, m, menthyl protons and OH), 3.15 (1H, dd, J 15.6 and 6.0 Hz, CH_2), 3.38 (1H, dd, J 6.3 and 6.0 Hz, CH), 3.54 (1 H, d, J 15.6 Hz, CH_2), 4.43 (1H, d, J 6.3 Hz, CH), 7.13-7.46 (4H, m, aromatics).

Reaction of the ylides 2 with 1,4-diphenylbutadiene in the presence of acenaphthylene

A solution of the ylide **2a** (1.00 g, 2.46 mmol), acenaphthylene (0.37 g, 2.46 mmol) and diphenylbutadiene (0.51 g, 2.47 mmol) in CH_2Cl_2 (10 ml) was stirred at room temperature overnight. A white crystalline precipitate forms. The mixture was chromatographed directly (hexane:CH_2Cl_2, 1:1) to give firstly the acenaphthylene adduct (0.58 g, 70%), m.p. 173-174°C (lit. m.p. 173-174°C)[3] followed by **4a** (an inseparable diastereoisomeric mixture) as a colourless oil (0.41 g, 38%), ν_{max} (liquid film) 1685 (CO) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.75-2.30 (18H, m,

aliphatic menthyl protons), 4.70 (1H, dt, J 10 Hz, CHO-), 4.95 (1H, m, CH), 5.90 (1H, m, CH), 6.10-6.40 (2H, m, 2 x CH), 7.15-7.70 (10H, m, aromatics).

Similarly, reaction of ylide **2b** gave adduct **4b** as a yellow oil (59%), ν_{max} (liquid film) 1685 (CO) cm^{-1}; δ_H (90 MHz, $CDCl_3$) 0.80-1.90 (16H, m, aliphatic fenchyl protons), 4.45 (1H, bs, CHO-), 5.00 (1H, m, CH), 5.95 (1H, m, CH), 6.10-6.40 (2H, m, 2 x CH), 7.20-7.70 (10H, m, aromatics).

X-Ray Crystallographic Analysis

Data for **6a** and **10a** were collected at room temperature on an Enraf Nonius CAD4 diffractometer. The relevant details are summarised in Table 1.

Table 1 Crystallographic details of compounds 6a and 10a

	Compound 6a	Compound 10a
Crystal size /mm	0.09 x 0.15 x 0.37	0.05 x 0.07 x 0.70
a /Å	8.374(2)	6.877(4)
b /Å	20.888(4)	11.061(3)
c /Å	10.041(2)	30.398(8)
β /°	95.90(2)	90.0
V /$Å^3$	1747(1)	2312
Space group	$P2_1$	$P2_12_12_1$
Z	4	4
F(000)	776	880
μ /cm^{-1}	5.86	3.58
Dcalc /g cm^{-3}	1.42	1.23
θ range /°	3-28	3-23
ω:2θ	3:1	1:1
Scan speed /° min^{-1}	variable, max = 3.30	variable, max = 3.30
Scan angle /°	0.54 + 0.34 tan θ	0.77 + 0.34 tan θ
h	0 → 11	0 → 7
k	0 → 27	0 → 12
l	-13 → 13	0 → 33
Reflections measured	4316	1908
Reflections used (F > 0)	3846	1323
Parameter refined	400	70
ρ_{max} /e$Å^{-3}$	0.35	0.77
$R = \sum\|\|Fo\|-\|Fc\|\|/\sum\|Fo\|$	0.066	0.180

The diffraction intensities were corrected for Lorentz and polarisation effects. An empirical absorption correction was applied for **6a**, and the data of **10a** were corrected for crystal decay (36%).

Both structures were solved with direct methods[16] and refined with SHELX76,[17] using blocked matrix (**6a**) and full-matrix (**10a**) least-squares methods. Non-hydrogen atoms were refined anisotropically for **6a** and isotropically for **10a**; the hydrogen atoms were included in calculated positions with a common isotropic thermal parameter that refined to U_{iso} = 0.105(9)$Å^2$ for **6a** and 0.12(3)$Å^2$ for **10a**. There are two molecules of compound **6** in the asymmetric unit, called A and B, with the numbering scheme indicated in the perspective drawing[18] of one molecule (A) shown in Figure 1. A spurious atom, probably crystal water, was found in **10a**. The molecule is depicted in Figure 2.

The scattering factors were taken from International Tables for Crystallography.[19] The final fractional atomic coordinates,* structure factors, thermal parameters, bond lengths and bond angles have been deposited with the Editors as supplementary data.

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The atomic coordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full citation for this paper.

Supplementary data and structural factors are available. See notice to Authors: Tetrahedron, 1984, 40(2), ii.