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THE GENERATION OF 2,3-DIHYDRO-2,3-bis-(METHYLENE)THIOPHENES FROM 4,6-DIHYDROTHIENO[3,4-b]THIOPHENE 5,5-DIOXIDES

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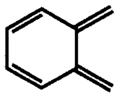
SUMMARY: On heating in sulpholane 4,6-dihydrothieno[3,4-b]thiophene 5,5-dioxides give 2,3-dihydro-2,3-bis(methylene)thiophenes which can be intercepted in Diels-Alder reactions. Sulphur dioxide is a very efficient trap for these thiophene xylylenes giving the cyclic sulphones by cheletropic addition.

There is currently considerable interest in heterocyclic analogues of *o*-xylylene (1)[1] and several reports of the generation of the thiophene derivative (2), both in solution[2] and by flash pyrolysis[3], have appeared. The high reactivity of this species and its tendency to polymerise when produced in high local concentration makes the former approach preferable where intermolecular trapping is desired.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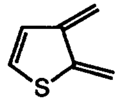
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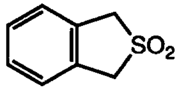

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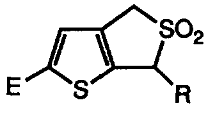
The cyclic sulphone (3) undergoes cheletropic extrusion of sulphur dioxide on heating in a solvent at high temperature.[4] This is a versatile type of precursor because the sulphone structure allows functionalisation of the methylene CH$_2$ groups via the stabilised α-sulphonyl anions[5] and this has been applied elegantly in steroid synthesis.[5b,c] We now report that this approach to xylylenes can be applied to the thiophene system and that this has important implications for the generation and handling of other heterocyclic xylylenes because these react readily with sulphur dioxide to give sulphones.

The cyclic sulphone (4; R = H, E = CO$_2$Me) is readily available by bischloromethylation of methyl thiophene-2-carboxylate, treatment with sodium sulphide and oxidation to the dioxide.[6] Heating in sulpholane at 200°C in the presence of a range of dienophiles gives the thiophene xylylene (5) - Diels-Alder adducts in good yield (Table)[7].

Methylation of the sulphone (4; R = H, E = CO$_2$Me) using lithium diisopropylamide (1.1 equiv.) and methyl iodide (1.1 equiv.) gave a single monomethyl derivative for which ^{1}Hmr data were consistent with the expected 6-methyl isomer (4; R = Me, E = CO_2Me). The 6-anion should be formed in preference to the 4-anion by virtue of the additional stabilising effect of the 2-ester group.[5b] Heating of this methyl sulphone in sulpholane in the presence of N-phenylmaleimide gave the adduct (6; R = Me, E = CO_2Me, X = NPh), (70%), formed by *endo* addition to the E-xylylene (5; R = Me, E = CO_2Me)[8]. No vinylthiophene (7) was observed, this being consistent with extrusion of sulphur dioxide leading preferentially to the less hindered E-isomer for which a competing 1,5-sigmatropic H migration is precluded.

The cycloaddition of sulphur dioxide to thiophene xylylenes is also a very efficient reaction. Thus the thiophene xylylene (2) generated flash pyrolytically from 2-chloromethyl-3-methylthiophene[3] is trapped (62%) by co-condensation with sulphur dioxide at -196°C followed by warming to room temperature. That this adduct is the cyclic sulphone (4; R = E = H) is confirmed by comparison of its ^{1}Hmr spectrum with that reported by Wynberg and Zwanenburg[9], who obtained the compound by bromodecarboxylation of the acid (4; R = H, E = CO_2H), and by our own independent synthesis from the cyclic sulphide (8)[10] by oxidation with peracetic acid. The thiophene xylylene (2) therefore differs from o-xylylene itself which gives mainly the Diels-Alder adduct (9) with sulphur dioxide under conditions of kinetic control[11].



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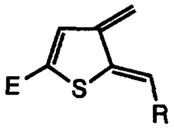

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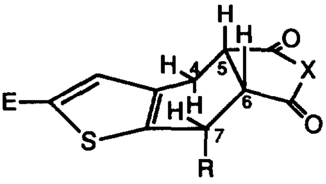

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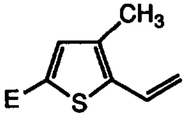

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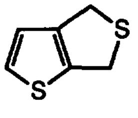

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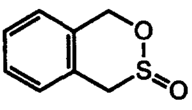

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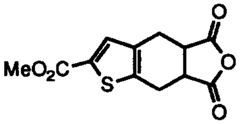
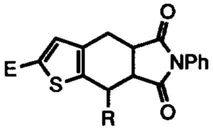
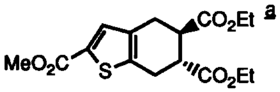
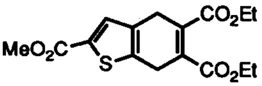
On heating in sulpholane with N-phenylmaleimide the cyclic sulphone (4; R = E = H) gave the expected Diels-Alder adduct of thiophene xylylene (2); this was identical with that reported from alternative precursors to xylylene (2).[2a] This result has important implications for the generation of other heterocyclic xylylenes, a number of which can be generated by flash pyrolysis of simple, readily available precursors[1]. A weakness of the flash pyrolytic approach is that the more reactive xylylenes, including (2), undergo rapid polymerisation rather than Diels-Alder addition even when the pyrolysate is co-condensed with dienophiles[1,3]. However, sulphur dioxide appears to be an especially reactive trapping agent, intercepting the thiophene xylylene

(2) and other heterocyclic xylylenes[1] when the flash pyrolysates are co-condensed with sulphur dioxide. Regeneration of the thiophene xylylene (2) from the pyrolytically produced adduct by

heating in solution and its successful trapping in Diels-Alder reactions suggests that this may also be possible with the other heterocyclic xylylenes. Thus the potential of flash pyrolysis for the generation of o-xylylenes is extended considerably by this sequence of pyrolysis, trapping with sulphur dioxide and extrusion in solution.

TABLE

XYLYLENE (5)	DIENOPHILE	ADDUCT	YIELD %	MP °C
E = CO_2Me, R = H	Maleic Anhydride		80	190-192
E = CO_2Me, R = H	N-Phenylmaleimide		78	168-170
E = CO_2Me, R = Me			92	187-188
E = H, R = H			70	164-165
E = CO_2Me, R = H	Diethyl Fumarate		85	74-75
E = CO_2Me, R = H	Diethyl Acetylene-dicarboxylate		85	75-77

[a] racemate

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REFERENCES AND NOTES

1. P.M.S. Chauhan, A.P.A. Crew, G. Jenkins, R.C. Storr, S.M. Walker and M. Yelland, *Tetrahedron Lett.*, preceding paper, and references therein.

2. (a) D.J. Chadwick and A. Plant, *Tetrahedron Lett.*, 1987, **28**, 6085; (b) A.M. van Leusen and K.J. van den Berg, *ibid.*, 1988, **29**, 2689.

3. P.M.S. Chauhan, G.Jenkins, S.M. Walker and R.C. Storr, *Tetrahedron Lett.*, 1988, **29**, 117.

4. M.P. Cava and A.A. Deana, *J. Am. Chem. Soc.*, 1959, **81**, 4266.

5. (a) W. Oppolzer, D.A. Roberts and T.G.C. Bird, *Helv. Chim. Acta*, 1979, **62**, 2017; (b) W. Oppolzer and D.A. Roberts, Helv. Chim. Acta, 1980, **63**, 1703; (c) K.C. Nicolaou, W.E. Barnette and P. Ma, *J. Org. Chem.*, 1980, **45**, 1463.

6. D.J. Zwanenburg, H. De Haan and H. Wynberg, *J. Org. Chem.*, 1966, **31**, 3363.

7. The sulphone (4) and dienophile (2.0 equivalents) were heated for 3h at 200°C in sulpholane and the adducts isolated by pouring into water, filtration/extraction and recrystallisation. All adducts gave satisfactory analytical and mass spectral data and showed the expected ^{1}Hmr absorptions. For example, the adduct with maleic anhydride (6; R = H, E = CO_2Me, X = O): δ $CDCl_3$ 7.57(s, H-3), 3.88 (s, CO_2Me), 3.67 (m, H-5,6), 3.45 (dd, H-7_{anti}), 3.32 (dd, H-4_{anti}), 3.07 (dd, H-7_{syn}) and 2.88 (dd, H- 4_{syn}), $J_{4anti,4syn}$ and $J_{7anti,7syn}$ = 15Hz; $J_{4syn,5}$ and $J_{7syn,6}$ = 6.5Hz; $J_{4anti,5}$ and $J_{7anti,6}$ = 2Hz. (Anti and syn refer to the configuration relative to the anhydride ring; the preferred conformation is as shown in 6).

8. *Endo* addition to the E-xylylene leads to the stereochemistry and preferred conformation shown in (6). The ^{1}Hmr signal for H-7_{syn} in the unmethylated adduct (6; R = H, E = CO_2Me, X = NPh) appears at δ 3.07. The corresponding signal in (6; R = Me, E = CO_2Me, X = NPh) is absent and a methyl doublet appears at δ 1.65.

9. D.J. Zwanenburg and H. Wynberg, *Rec. Trav. Chim.*, 1969, **88**, 321.

10. D.W.H. MacDowell and T.B. Patrick, *J. Org. Chem.*, 1966, **31**, 3592.

11. T. Durst and L. Tétreault-Ryan, *Tetrahedron Lett.*, 1978, **26**, 2353.

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