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Preparation and Cycloaddition Reactions of Silylated Thiophene 1,1-Dioxides.

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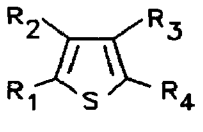
Abstract: **Methods of preparation of the four bis(trimethylsilyl)thiophene isomers and 2,3,5-tris(trimethylsilyl)thiophene are described; the corresponding dioxides are versatile intermediates for the Diels-Alder reaction.**

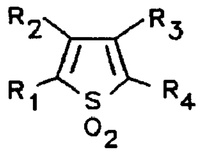
The use of thiophene 1,1-dioxides as diene equivalents in cycloaddition reactions is restricted by the limited stability of the majority of simple derivatives of the system. Thiophene dioxide itself cannot be isolated owing to dimerisation, though it has been generated in dilute solution.[1-4] While a potent dienophile, it showed limited reactivity as an electron deficient diene.[1,2] Attempts to prepare monosubstituted thiophene dioxides have also been unsuccessful, and only on moving to the disubstituted and higher derivatives do such compounds become stable enough to permit general isolation.[5] We reasoned that the trimethylsilyl substituent should be bulky enough to prevent dimerisation of the corresponding thiophene dioxides and, by virtue of the lability of the silyl group towards both electrophilic and nucleophilic reagents,[6,7] would offer a convenient route to further functionalisation of the envisaged adducts. Following initiation of this work, preparations of 2,5-bis(trimethylsilyl)thiophene dioxide[8] and some derivatives of 3-trimethylsilylthiophene dioxide[9] have been described elsewhere; however the behaviour of these systems in cycloaddition reactions has not been reported.

The only bis(trimethylsilyl)thiophene described in the literature is the 2,5-isomer **3**.[8] We initially prepared this compound by lithium-halogen exchange from 2,5-dibromothiophene followed by treatment with chlorotrimethylsilane at -70 °C, but have since established that 2,5-dilithiothiophene is more conveniently obtained by direct lithium-hydrogen exchange from thiophene using n-butyllithium in ether at room temperature. An analogous lithiation followed by trimethylsilylation of 3-trimethylsilylthiophene[10] gave the previously unreported 2,4-bis(trimethylsilyl)thiophene **2**[11,12] in quantitative yield. The exclusive formation of this isomer over the 2-substitution product **1** is probably more a consequence of the electron releasing properties of the 3-substituent (and the concomitant higher relative acidity of 5-H) than a simple steric effect, as further lithiation/silylation of **2** under the same conditions gave 2,3,5-tris(trimethylsilyl)thiophene **5**. The latter compound cannot be prepared from 2,5-bis(trimethylsilyl)-3-bromothiophene[13] as silylation of the lithiation product is not competitive with C(5)-S bond cleavage (at ca. -20 °C), giving the silylated enyne thioether **6** as the exclusive product. An analogous enyne was obtained upon reaction of chlorotrimethylsilane with 3-lithio-2-trimethylsilylthiophene, but the 2,3-substitution product **1** can be obtained in moderate yield by use of the more reactive iodotrimethylsilane. Attempts to prepare 3,4-bis(trimethylsilyl)thiophene **4** by dilithiation of 3,4-dibromothiophene with n-butyllithium followed by disilylation proved unsuccessful; however this compound can be obtained by sequential low-temperature silylations, the second lithiation step involving treatment of 3-bromo-4-trimethylsilylthiophene with two equivalents of t-butyllithium. In contrast to the 2,4-isomer, 3,4-bis(trimethylsilyl)thiophene does not undergo further lithium-hydrogen exchange at room temperature; the combined blocking effect of two bulky β-substituents appears to be sufficient to prevent approach of the solvated alkyl (methyl-, n-butyl- or t-butyl) lithium complex to the α-position. This has as yet thwarted our attempts to prepare 2,3,4-tris(trimethylsilyl)thiophene and 2,3,4,5-tetrakis(trimethylsilyl)thiophene; we are currently investigating alternative routes to these hindered systems.



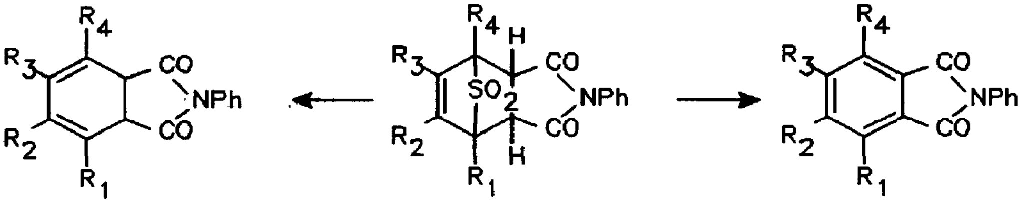
1 R_1R_2 = $SiMe_3$, R_3R_4 = H
2 R_1R_3 = $SiMe_3$, R_2R_4 = H
3 R_1R_4 = $SiMe_3$, R_2R_3 = H
4 R_2R_3 = $SiMe_3$, R_1R_4 = H
5 $R_1R_2R_4$ = $SiMe_3$, R_3 = H

6



7 R_1R_2 = $SiMe_3$, R_3R_4 = H
8 R_1R_3 = $SiMe_3$, R_2R_4 = H
9 R_1R_4 = $SiMe_3$, R_2R_3 = H
10 R_2R_3 = $SiMe_3$, R_1R_4 = H
11 $R_1R_2R_4$ = $SiMe_3$, R_3 = H

The trimethylsilylthiophenes are readily oxidised at room temperature, by aqueous peracetic acid or m-chloroperbenzoic acid in dichloromethane, without displacement of the silyl substituents. Stable dioxides could not be isolated from either of the monotrimethylsilylthiophenes; these compounds form mixtures of dimers, the structures of which will be described at a future date. The dioxides **7-11** of the bis(trimethylsilyl)thiophenes and 2,3,5-tris(trimethylsilyl)thiophene are colourless crystalline solids which are thermally stable to temperatures in excess of 200 °C. In keeping with the loss of aromatic character of the thiophene nucleus, the ring hydrogens in **7-11** all show a shift to high field in their ^1H n.m.r. spectra,[12] this being particularly pronounced for protons occupying an α-position.

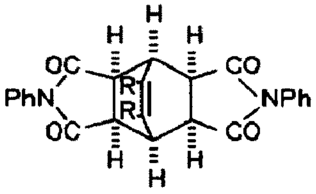


12 R_1R_3 = $SiMe_3$, R_2R_4 = H
13 R_1R_4 = $SiMe_3$, R_2R_3 = H
14 R_2R_3 = $SiMe_3$, R_1R_4 = H
15 $R_1R_2R_4$ = $SiMe_3$, R_3 = H

16 R_1R_3 = $SiMe_3$, R_2R_4 = H
17 R_1R_4 = $SiMe_3$, R_2R_3 = H
18 R_2R_3 = $SiMe_3$, R_1R_4 = H

2,4-Bis(trimethylsilyl)thiophene dioxide **8** and the 2,5-isomer **9** give the mono-adducts **12** and **13** in high yield on reaction with N-phenylmaleimide in refluxing *o*-xylene. The intermediate sulphone adducts could not be isolated, undergoing elimination of sulphur dioxide at the temperatures used. When the same reactions were carried out in DMF solvent the corresponding aromatisation products **16** and **17** were obtained in yields of 75 and 82% respectively, and the dihydro derivatives **12** and **13** could not be detected. While the unsymmetrical adduct **12** does undergo slow aerial oxidation to **16**, the 2,5-adduct **13** can be recovered unchanged after boiling in DMF. We infer that the aromatisation products are likely to form via an E_{1cb} mechanism in basic solvents, by proton abstraction from a position α to a carbonyl group and β to a silyl substituent. The subsequent C-S bond cleavage step appears to be facilitated by an adjacent silyl substituent, providing a convenient route to a variety of novel silylated aromatic systems.

3,4-Bis(trimethylsilyl)thiophene dioxide formed the diadduct **19** on treatment with N-phenylmaleimide in refluxing *o*-xylene; the anticipated mono-adduct **14** could not be detected. This product is presumed to have the illustrated *endo,endo*-geometry, the ^{1}H n.m.r. spectrum showing signals at δ 0.19 (18 H, s, -CH_3), 3.14 (4 H, t, 1-, 2-, 4-, 5-H, $J_{2,3}$ 1.50 Hz), 4.23 (2 H, t, 3-, 6-H), and 7.19-7.49 (10 H, m, -Ph), while the ^{13}C spectrum excluded the *endo,exo*-isomer, showing only two saturated carbon environments for the central ring at δ 38.0 and 42.7. It is noteworthy that the recently reported 3,4-bis(t-butyl)thiophene dioxide has only been reported to form mono-adducts on reaction with dienophiles.[14] In DMF solvent the dioxide **10** and N-phenylmaleimide gave a mixture of the diadduct **19** (27%) and the aromatisation product **18** (15%), the relatively low yield of the latter product presumably reflecting that no α-silyl substituent is available to facilitate C-S bond cleavage.



19 R = $SiMe_3$

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11 All new compounds gave satisfactory mass spectra and elemental analyses.
12 Selected data (^{1}H and ^{13}C n.m.r. spectra in $CDCl_3$ at 250 and 62.89 MHz respectively, J values in Hz). Other than for compounds **2**, **4**, **5** and **6**, yields have not been optimised: **1**: pale yellow oil (35%), δ_H 0.33 (9 H, s, -CH_3), 0.40 (9 H, s -CH_3), 7.36 (1 H, d, 4-H, $J_{4,5}$ = 4.6), 7.58 (1 H, d, 5-H); **2**:

colourless oil (96%), δ_H 0.27 (9 H, s, -CH_3), 0.33 (9 H, s, -CH_3), 7.29 (1 H, d, 3-H, $J_{3,5}$ = 0.75), 7.67 (1 H, d, 5-H); δ_C -0.40, 0.16 (2CH_3), 136.6, 138.5 (C-3, -5); **4**: colourless oil (74%), δ_H 0.33 (18H, s, -CH_3), 7.59 (2H, s, 2-, 5-H); δ_C 1.06 (CH_3) and 134.7 (C-2, -5); **5**: m.p. 41-42 °C (65%), δ_H 0.33 (9 H, s, -CH_3), 0.34 (9 H, s, -CH_3), 0.40 (9 H, s, -CH_3), 7.46 (1 H, s, 4-H); δ_C 0.26, 1.38, 1.64 (3CH_3), 143.0 (C-4); **6**: colourless oil (80%), δ_H 0.15 (9 H, s, -CH_3), 0.21 (9 H, s, -CH_3), 0.37 (9 H, s, -CH_3), 6.41 (1 H, s, 3-H); δ_C -1.68, 0.05, 0.37 (3CH_3), 102.6, 103.7 (C-4, -5), 126.7 (C-3), 150.1 (C-1); **7**: m.p. 113-115 °C (54%), δ_H 0.31 (9 H, s, -CH_3), 0.43 (9 H, s, -CH_3), 6.69 (1 H, d, 5-H), 6.84 (1 H, d, 4-H, $J_{4,5}$ = 6.3); **8**: m.p. 116-118 °C (74%), δ_H 0.24 (9 H, s, -CH_3), 0.36 (9 H, s, -CH_3), 6.68 (1 H, d, 5-H), 6.74 (1 H, d, 3-H, $J_{3,5}$ = 0.57); δ_C -2.49, -1.71 (2CH_3), 136.6, 138.5 (C-3, -5); **10**: m.p. 115-117 °C (94%), δ_H 0.30 (18 H, s, -CH_3), 6.68 (2 H, s, 2-, 5-H); δ_C -0.34 (-CH_3), 137.1 (C-2, -5); **11**: m.p. 70-75 °C (80%), δ_H 0.31 (9 H, s, -CH_3), 0.34 (9 H, s, -CH_3), 0.41 (9 H, s, -CH_3), 6.78 (1 H, s, 4-H); δ_C -1.65, -0.27, 0.33 (3CH_3), 140.1 (C-4); **12**: m.p. 103-105 °C (76%), δ_H 0.13 (9 H, s, -CH_3), 0.24 (9 H, s, -CH_3), 3.78 (1 H, dd, 1-H, $J_{1,2}$ =12.1, $J_{1,6}$ = 3.7), 3.95 (1 H, d, 2-H), 6.04 (1 H, d, 6-H), 6.39 (1 H, s, 4-H), 7.30-7.36 (5 H, m, -Ph); **13**: m.p. 148-149 °C (83%), δ_H 0.21 (18 H, s, -CH3), 3.96 (2 H, s, 1-, 2-H), 6.36 (2 H, s, 4-, 5-H), 7.24-7.49 (5 H, m, -Ph); **15**: m.p. 138-140 °C (50%), δ_H 0.21 (9 H, s, -CH_3), 0.26 (9 H, s, -CH_3), 0.33 (9 H, s, -CH_3), 3.85 (1 H, dd, 1-H, $J_{1,2}$ = 10.5, $J_{1,5}$ = 2.5), 4.06 (1 H, d, 2-H), 6,57 (1-H, d, 5-H), 7.28-7.43 (5 H, m, -Ph); **16**: m.p. 120-121 °C (75%), δ_H 0.36 (9 H, s, -CH_3), 0.44 (9 H, s, -CH_3), 7.36-7.55 (5 H, m, -Ph), 8.06 (1 H, d, 4-H, $J_{4,6}$ = 1.0), 8.11 (1 H, d, 6-H); **17**: m.p. 147-148 °C (82%), δ_H 0.42 (18 H, s, -CH_3), 7.36-7.55 (5 H, m, -Ph), 7.85 (2 H, s, 4-, 5-H); **18**: m.p. 185-186 °C (15%), δ_H 0.45 (18 H, s, -CH_3), 7.37-7.55 (5 H, m, -Ph), 8.21 (2 H, s, 3-, 6-H); **19**: m.p. > 350 °C (27%), n.m.r. spectra, see text.

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