Control of Regioselectivity in the Alkylation of 2-Trimethylsilyl-2,5-dihydrothiophene 1,1-Dioxide. A Route for 2,2-Dialkylation

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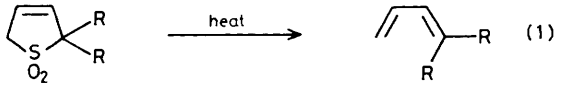
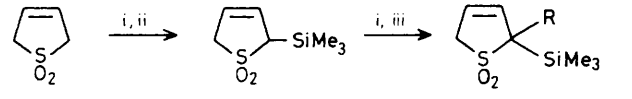
The readily available 2-trimethylsilyl-2,5-dihydrothiophene 1,1-dioxide can be converted regioselectively into the dialkyl- and dispiro analogues, which are precursors of the corresponding 1,1-disubstituted buta-1,3-dienes and asymmetric dicycloalkylidenylethanes, respectively.

During studies of the synthetic applications of the direct deprotonation–alkylation reaction of 2,5-dihydrothiophene 1,1-dioxides,[1] we and others have found that one-pot or stepwise dialkylation reactions regioselectively give the 2,5-disubstituted analogues,[2] but regioselective control of 2,2-dialkylation directly from (**1**) has never been achieved. The thermolysis of the 2,2-disubstituted products to give the corresponding disubstituted buta-1,3-dienes is well established, (reaction 1).[3] We hereby describe an attractive and convenient method for the synthesis of these compounds from the 2-trimethylsilyl derivative (**2**).

Compound (**2**) was synthesized in 43% yield by treatment of the anion of (**1**) with Me_3SiCl–NaI in tetrahydrofuran (THF)–hexamethylphosphoramide (HMPA).[4] The yield can be improved to 70% by using Me_3SiI in THF (Scheme 1). When (**2**) in THF was treated with Bu^nLi (1 equiv., −105 °C) and then with MeI (1 equiv.), the 2-methyl-2-trimethylsilyl analogue (**3a**) was produced in 85% yield (Scheme 1). If 2.5 equiv. of MeI were used and HMPA was added as cosolvent in the same sequence, (**3a**) was formed along with the 2,2-dimethyl compound (**5a**) and the 2-methyl compound (**6a**) in

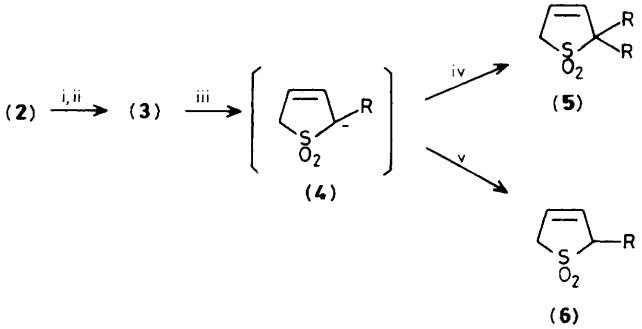


(1)



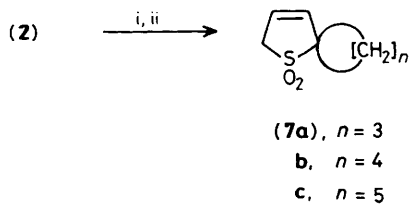
(**1**) (**2**) (**3a**); R = Me

Scheme 1. *Reagents and conditions:* i, Bu^nLi, THF, −105 °C; ii, Me_3SiI; iii, MeI (1 equiv.).

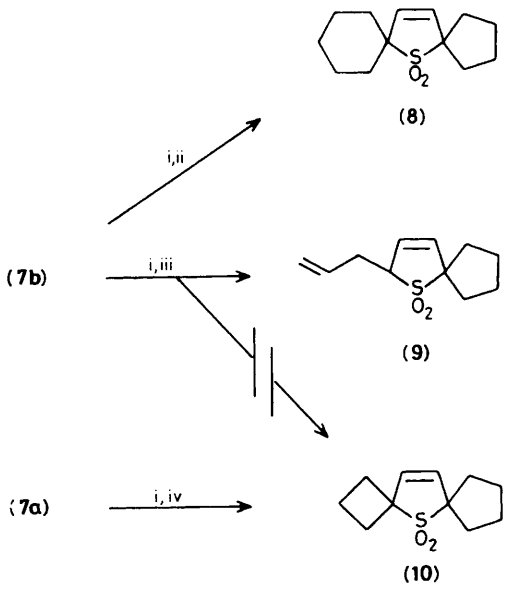


a; R = Me
b; R = Et

Scheme 2. *Reagents and conditions:* i, Bu^nLi, THF–HMPA, −105 °C; RI (2.5 equiv.); iii, I^-; iv, RI; v, H_2O.



Scheme 3. *Reagents and conditions:* i, Bu^{n}Li, THF–HMPA, −105 °C; ii, I–[CH$_2$]$_n$–I, −105 °C reflux.



Scheme 4. *Reagents and conditions:* i, LiHMDS, THF–HMPA, −78 °C; ii, I–[CH$_2$]$_5$–I; iii, I–[CH$_2$]$_3$–I; iv, I–[CH$_2$]$_4$–I.

2:1:1 ratio. No starting material or other products were found in any significant quantity (Scheme 2). Compounds (**5a**) and (**6a**) must be formed by a second methylation or a protonation, respectively, from anion (**4a**) generated by iodide attack on the trimethylsilyl group of (**3a**).

On refluxing the reaction mixture overnight, (**5a**) was obtained as the major product in 52% yield. With EtI in place of MeI, (**5b**) was formed in 61% yield. Using an α,ω-di-iodoalkane as the alkylating agent, spiro compounds (**7a**) (47%), (**7b**) (52%), or (**7c**) (56%) could also be produced (Scheme 3). However, a similar reaction with 1,2-di-iodo-ethane proved to be complex and no cyclized product was observed. Further intramolecular dialkylations of (**7a**,**b**,**c**) with other α,ω-di-iodoalkanes were expected to yield asymmetric dispirocyclic products. Since dicyclohexylidene-ethane is known to be produced in quantitative yield by the thermolysis of the symmetrical 7-thiadispiro[5.1.5.2]penta-dec-14-ene 7,7-dioxide,[2] it was reasonable to expect the asymmetric dispirocyclic compounds to be precursors of asymmetric dicycloalkylidene-ethanes. When (**7b**) in THF–HMPA was treated with lithium hexamethyldisilazide (LiHMDS) (2 equiv.) and 1,5-di-iodopentane (1 equiv.), the asymmetric dispirocyclic compound (**8**) was produced in 61% yield (Scheme 4). Interestingly, the reaction of (**7b**) with 1,3-di-iodopropane resulted in the formation of the elimination product (**9**) instead of the dispiro-compound (**10**) (Scheme 2). However, (**10**) was obtained in 65% yield by the reaction of (**7a**) with 1,4-di-iodobutane.

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