Regioselective Synthesis of 3-Acylated 2,5-Dihydrothiophene *S,S*-Dioxides *via* Ultrasound-promoted Allylzincation of 3-Bromo-2,3-dihydrothiophene *S,S*-Dioxide

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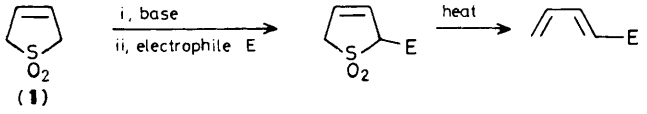
3-Acylated 2,5-dihydrothiophene *S,S*-dioxides were synthesized from 3-hydroxyalkylated 2,3-dihydrothiophene *S,S*-dioxides, prepared highly regioselectively *via* ultrasound-promoted allylzincation of 3-bromo-2,3-dihydrothiophene *S,S*-dioxide.

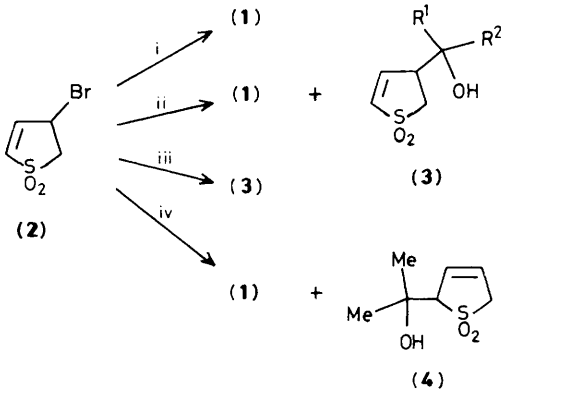
During studies of the synthetic application of direct deprotonation–substitution reactions of 2,5-dihydrothiophene *S,S*-dioxide (**1**),[1] we have successfully prepared alkylated,[1a] acylated,[1b] and silylated[1c] derivatives, which are stable precursors of the corresponding substituted buta-1,3-dienes. However, all these reactions are limited to attaching electrophiles regioselectively to the α-position of the *S,S*-dioxide; thus they can be used only in the preparation of 1-substituted butadienes (Scheme 1). γ-Substitutions have been observed only rarely,[1c,d] and have not been found synthetically useful. We have recently discovered that 3-hydroxyalkylated 2,3-dihydrothiophene *S,S*-dioxides can be prepared highly regioselectively from the readily available 3-bromo-2,3-dihydrothiophene *S,S*-dioxide (**2**)[2] and carbonyl compounds *via* an allylzincation process. These intermediate alcohols can then be oxidized to 3-acylated 2,5-dihydrothiophene *S,S*-dioxides, which are the stable precursors of 2-acylated buta-1,3-dienes.[3]

Recently, allylations of aldehydes and ketones, to produce homoallylic alcohols have attracted renewed interest.[4] In the light of this work, we expected that compound (**2**), bearing an allylic bromide functionality, would be able to react with carbonyl compounds by zincation. When compound (**2**) (1 equiv.) was treated *in situ* with zinc powder (1.2 equiv.) and acetone (1.4 equiv.) in tetrahydrofuran (THF) under reflux overnight, a trace of γ-substituted product (**3a**) was formed along with compound (**1**) as the major product. Compound (**1**) was obtained almost in quantitative yield in the absence of acetone. With a slight modification of the reaction conditions, using Zn–Ag[5] instead of Zn, the yield of (**3a**) could be raised to 33.4%, but this was still not considered satisfactory. [In no case was the α-substituted product (**4**) detected.] However, application of ultrasonic irradiation[6] instead of refluxing dramatically improved the results. Thus, the product (**3a**) was produced cleanly in 88.9% yield when a mixture of (**2**), acetone, and Zn–Ag was sonicated in a laboratory cleaning bath (Branson, 50—60 Hz, 125 W) at room temperature for 5 h (Scheme 2). When the same conditions were used with other aldehydes and ketones, the corresponding alcohols (**3b—i**) were also obtained in high yields (Table 1). This procedure appears to be a good route for γ-substitution of dihydrothiophene dioxide anions. When magnesium powder was used in place of Zn–Ag in the reaction of (**2**) and acetone



(**1**)

Scheme 1. E = alkyl, acyl, trimethylsilyl.



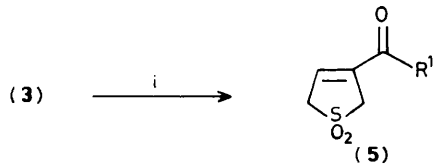
(**4**)

Scheme 2. *Reagents:* i, Zn, THF, reflux; ii, Zn–Ag, $R^1R^2C{=}O$, THF, reflux; iii, Zn–Ag, $R^1R^2C{=}O$, THF, room temp., ultrasound; iv, Mg, Me_2CO, $HgCl_2$, THF, room temp., ultrasound.

Table 1. Reactions of the sulphone (**2**) with carbonyl compounds and the subsequent oxidation products.[a]

		Adducts (**3**)			Oxidation products (**5**)	
Carbonyl compounds		R^1	R^2	Yield (%)		Yield (%)
Me_2CO	**a**	Me	Me	88.9		
PhMeCO	**b**	Me	Ph	77.6		
Ph_2CO	**c**	Ph	Ph	35.4		
MeCHO	**d**	Me	H	97.5	**a**	51.4
EtCHO	**e**	Et	H	85.4	**b**	47.9
$[CH_2]_5CHCHO$	**f**	$[CH_2]_5CH$	H	79.7	**c**	49.8
PhCHO	**g**	Ph	H	86.7	**d**	49.5
$CH_2{=}CH[CH_2]_2CHO$	**h**	$CH_2{=}CH[CH_2]_2$	H	87.5	**e**	46.6
$CH_2{=}CH[CH_2]_3CHO$	**i**	$CH_2{=}CH[CH_2]_3$	H	91.7	**f**	44.9

[a] All products, except (**5a**), are new and gave satisfactory spectroscopic (n.m.r., i.r., and mass) and/or analytical data; (**3b**) and (**3e—i**) are mixtures of diastereomers and could not be separated.



Scheme 3. *Reagents:* i, pyridinium chlorochromate, molecular sieves (3 Å), THF, 35 °C.

with $HgCl_2$ as initiator, the regiochemistry was completely reversed. The α-substituted product (**4**) was obtained (30.6%), accompanied by (**1**) and starting material (**2**); no (**3a**) was formed. Compound (**4**) was recently synthesized directly from (**1**).[7] This result raises the possibility of using a counter-ion effect to control regioselectivity of substitution of dihydrothiophene dioxide anions.

When compound (**3d**) (1 equiv.) was treated with pyridinium chlorochromate and molecular sieves (3 Å; 6.5 equiv.) in THF at 35 °C for 1.5 h, smooth oxidation took place accompanied by double bond migration to give 3-acetyl-2,5-dihydrothiophene *S,S*-dioxide (**5a**) (Scheme 3). The n.m.r. and i.r. spectral data for the product (**5a**) were identical with those reported.[3] Similarly, compounds (**3e—i**) were oxidized to the corresponding 3-acylated 2,5-dihydrothiophene *S,S*-dioxides (**5b—f**) (Table 1).

Since compound (**2**) is readily available and the conditions for allylzincation and oxidation reactions are very mild, the reaction sequence described here constitutes an attractive route to 3-acylated 2,5-dihydrothiophene *S,S*-dioxides, of which (**5a**) has been demonstrated to be a precursor of 2-acetyl-buta-1,3-diene.[3] In this respect, compound (**2**) serves as a convenient buta-1,3-diene 2-anion equivalent.

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