

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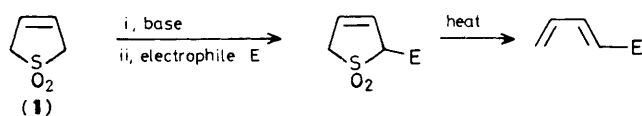
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3-Acylated 2,5-dihydrothiophene *S,S*-dioxides were synthesized from 3-hydroxyalkylated 2,3-dihydrothiophene *S,S*-dioxides, prepared highly regioselectively *via* ultrasound-promoted allylzincation of 3-bromo-2,3-dihydrothiophene *S,S*-dioxide.

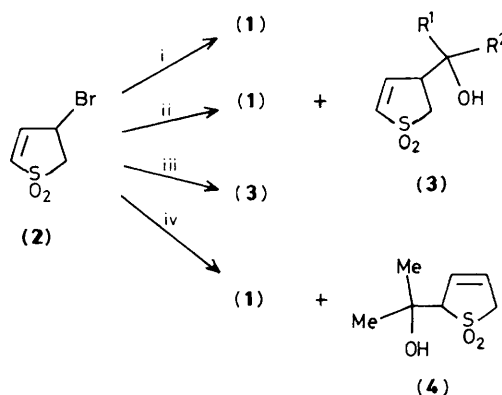
During studies of the synthetic application of direct deprotonation–substitution reactions of 2,5-dihydrothiophene *S,S*-dioxide (1),¹ we have successfully prepared alkylated,^{1a} acylated,^{1b} and silylated^{1c} derivatives, which are stable precursors of the corresponding substituted buta-1,3-dienes. 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–Ag⁵ 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 irradiation⁶ 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



Scheme 1. E = alkyl, acyl, trimethylsilyl.

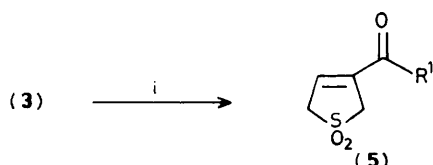


Scheme 2. Reagents: i, Zn, THF, reflux; ii, Zn–Ag, $R^1R^2C=O$, THF, reflux; iii, Zn–Ag, $R^1R^2C=O$, THF, room temp., ultrasound; iv, Mg, Me_2CO , $HgCl_2$, THF, room temp., ultrasound.

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

Carbonyl compounds	Adducts (3)			Oxidation products (5)	
		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-but-1,3-diene.³ In this respect, compound (2) serves as a convenient buta-1,3-diene 2-anion equivalent.

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