Complete Retention of Configuration in the Nucleophilic Substitution of 1-Phenylbenzo[*b*]thiophenium Salts by Alkoxide Anions

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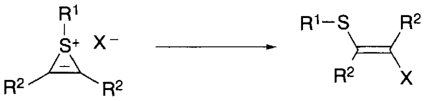
Reaction of 1,2,3-triarylbenzo[*b*]thiophenium salts with alkoxide anions results in the exclusive formation of (*Z*) alkoxy-substituted alkenes, indicating that the nucleophilic ring-opening reaction proceeds with complete retention of configuration.

Stereoselective nucleophilic substitution reactions are synthetically important processes. Generally, nucleophilic vinylic substitution proceeds *via* the multi-step processes such as addition–elimination and S_N1 reactions and results in a mixture of (*E*) and (*Z*) substituted alkenes.[1] Recent attention has been focused on the single step, *i.e.* S_N2 type reaction,[2] in addition to the multi step, *i.e.* addition–elimination process.[1f] Among the nucleophilic vinylic substitutions, the ring opening reaction of three-membered thiirenium salts[2a,b,d] has been discussed as a typical example of the single step processes. The reaction of the thiirenium salts with nucleophiles exclusively provides the (*E*) isomer of substituted alkenes, with complete inversion of configuration [eqn. (1)]. It is thought that the ring strain in the three-membered thiirenium salts makes them more susceptible to nucleophilic substitution. Thus, we conducted nucleophilic substitution of 1-phenylbenzo[*b*]thiophenium salts which have a strain-free five-membered ring and found that they behaved quite differently from the thiirenium salts in the reaction with nucleophilic alkoxide anions. In this paper we report a new type of nucleophilic substitution which proceeds with complete retention of configuration.

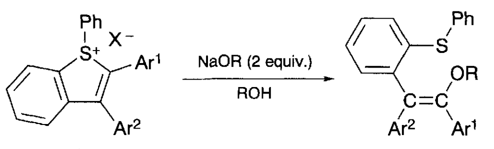


(1)

Although cyclic sulfonium salts have been reported,[3] very few benzothiophenium salts are known to react with nucleophiles to give substituted products, since most are alkylated and tend to undergo dealkylation with nucleophilic reagents and solvents. It has been previously proposed[4] that five-membered 1-methylbenzo[*b*]thiophenium ions are present as the intermediates in the intramolecular cyclization of β-[*o*-(methylsulfanyl)phenyl]vinyl cations but the intermediate 1-methylbenzo[*b*]thiophenium ions are demethylated by the counter anion to lead to benzothiophenes. On the other hand, β-[*o*-(phenylsulfanyl)phenyl]vinyl cations bearing a strong Ph–S bond give rise to the intermediate 1-phenylbenzo[*b*]thiophenium ions which can be isolated as stable salts.[5] Several substituted 1-arylbenzo[*b*]thiophenium salts have been prepared by a similar intramolecular cyclization[6] and by arylation of benzothiophenes.[7] X-Ray crystallographic analysis of some benzothiophenium salts shows some interesting features. The crystal structure of 1,2,3-triphenylbenzo[*b*]thiophenium perchlorate indicates that the Ph–S bond length is 1.784 Å and the other C–S bond lengths are 1.762 [C(7a)–S bond] and 1.790 Å [C(2)–S bond].[6] The short Ph–S bond reflects the reactivity of 1-phenylbenzo[*b*]thiophenium salts according to the rules of Jones and Kirby,[8] and Tidwell.[9] From the crystal data,[6] 1-phenylbenzo[*b*]thiophenium ions are regarded as the cyclic sulfonium ions of styrene derivatives, since 1,2,3-triphenylbenzo[*b*]thiophenium perchlorate has the pyramidal structure around the sulfur atom, and the short C–C double bond (1.346 Å) of the thiophene ring being in the range of typical double bond lengths of triarylvinyl systems (typically 1.32–1.35 Å).[10]

1,2,3-Triarylbenzo[*b*]thiophenium salts **1** were prepared from 1,2-diaryl-1-[*o*-(phenylsulfanyl)phenyl]ethenes.[6] Bromination of 1,2-diaryl-1-[*o*-(phenylsulfanyl)phenyl]ethenes in CH_2Cl_2 at 0 °C gave 1-phenyl-2,3-diarylbenzo[*b*]thiophenium bromides (**1**, X = Br) which were purified by column chromatography on alumina. The corresponding 1-phenylbenzo[*b*]thiophenium perchlorate (**1c**, X = ClO_4) was prepared by treatment of **1c** (X = Br) with $AgClO_4$.

A solution of 1,2,3-triarylbenzo[*b*]thiophenium salt **1** (0.5–1.0 mmol) in an alcohol (20 cm^3) in the presence of the corresponding alkoxide anion (1–2 mmol, 2 equiv.) was refluxed or heated for 12 h at the temperature shown in Table 1. The triarylbenzothiophenium salts **1** were quite stable in the presence of nucleophilic anions, even in the presence of hydroxide and methoxide anions at room temperature. After evaporation of the solvent, the product was isolated by column chromatography on alumina or silica gel then characterised as the alkoxy-1,2-diaryl-2-[*o*-(phenylsulfanyl)phenyl]ethenes **2** [eqn. (2)]. Interestingly, the ^1H and ^{13}C NMR spectra of the products **2** indicated that only one of the possible (*E*) and (*Z*) isomers was present. The isolated yields of the substituted alkoxyethenes **2** were quantitative or quite high as shown in Table 1. Even in the reactions with sterically bulky alkoxide anions such as sodium 2-propoxide and sodium 2,2-dimethylpropoxide, the substitution products **2** were obtained stereoselectively. The isomers produced in these reactions were stable in the crystalline state and did not change under refluxing conditions (12 h) in an alcohol containing the corresponding



(2)

1

a Ar¹ = Ar² = Ph
b Ar¹ = Ph, Ar² = An
c Ar¹ = An, Ar² = Ph
X = Br, ClO_4

2

a Ar¹ = Ar² = Ph
b Ar¹ = Ph, Ar² = An
c Ar¹ = An, Ar² = Ph ,
R = Me, Et, Pr^i, Me_3CCH_2

Table 1 Reaction of 1-phenylbenzothiophenium salts **1** with alkoxide anions

Benzothiophenium salt **1**			NaOR–ROH		
Ar¹	Ar²	X	R	*T*/°C	Alkoxyethene **2** yield (%)
Ph	Ph	Br	Me	Reflux	100 (**2a-Me**)
Ph	An[a]	Br	Me	Reflux	100 (**2b-Me**)
An[a]	Ph	Br	Me	Reflux	100 (**2c-Me**)
An[a]	Ph	ClO_4	Me	Reflux	100 (**2c-Me**)
An[a]	Ph	ClO_4	Et	Reflux	100 (**2c-Et**)
An[a]	Ph	ClO_4	Pr^i	Reflux	100 (**2c-Pr**)
An[a]	Ph	ClO_4	Me_3CCH_2	80	82[b] (**2c-Pen**)[c]

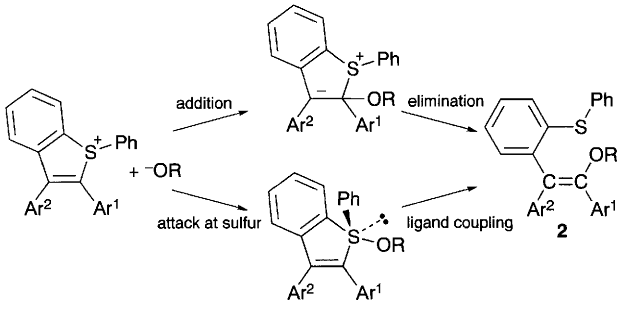
[a] An = *p*-Methoxyphenyl. [b] Some of the starting benzothiophenium salt **1** was also recovered. [c] Pen = neopentyl.

alkoxide anion. However, isomerisation occurred in the presence of a small amount of HCl within minutes. When the reaction of 2-(*p*-methoxyphenyl)-1,3-diphenylbenzo[*b*]thiophenium perchlorate **1c** (X = ClO_4) with a more bulky nucleophile, *tert*-butoxide anion, in *tert*-butyl alcohol was conducted under refluxing conditions, a complex mixture containing 30% of 2-(*p*-methoxyphenyl)-3-phenylbenzothiophene was obtained. The reaction with the bulky *tert*-butoxide anion seems to proceed *via* an electron transfer reaction followed by radical decomposition.[11]

The exclusive formation of 1-alkoxy-1,2-diaryl-2-[*o*-(phenylsulfanyl)phenyl]ethenes **2** was confirmed by NMR spectroscopy which showed only one isomer to be present. It was, however, difficult to determine the configuration of the alkoxyethenes **2** by spectral means. Accordingly, the absolute structure was analysed by a single crystal X-ray diffraction of 1-methoxy-2-(*p*-methoxyphenyl)-1-phenyl-2-[*o*(phenylsulfanyl)phenyl]ethene (**2b-Me**) which was obtained by a slow recrystallization. This confirmed that the obtained methoxyethene **2b-Me** had the (*Z*) configuration.[12] Consequently, the nucleophilic substitution of 1-phenylbenzo[*b*]thiophenium salts provides products with retention of stereochemistry.

The exclusive formation of the alkoxyethenes **2** with the (*Z*) configuration indicates that the nucleophilic substitution of 1-phenylbenzo[*b*]thiophenium salts **1** proceeds *via* a different mechanism from that of the thiirenium salts. The observed stereochemical outcome may be in accord with two mechanisms, *i.e.* the nucleophilic addition of alkoxide anions followed by a rapid elimination of the sulfur group[11] or a ligand coupling process on sulfur (Scheme 1).[13] Even with the bulky alkoxide anions, the nucleophilic substitution proceeds with complete retention of configuration. This result cannot be attributed to the thermodynamic stability of the (*E*) and (*Z*) alkoxyethenes.

In summary, we have found that strain-free five-membered 1-phenylbenzo[*b*]thiophenium salts **1** undergo nucleophilic substitution with compete retention of configuration. This result suggests that an in-plane S_N2 type reaction with inversion is possible where a cationic character is developed at the vinylic carbon.[2]



Scheme 1

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Footnote

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