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α- VERSUS β-CARBON NUCLEOPHILIC ATTACK IN VINYLIC SUBSTITUTION

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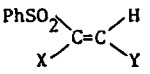
The mechanism of substitution of the bromine atom in (*Z*)-α-bromo-β-arylthiovinyl phenyl sulphones, $PhSO_2CBr{=}CHSAr$, with arylthiolates, $Ar'S^-$ was studied. The same mixture of the four possible products, $PhSO_2C(SAr'){=}CHSAr$ (Ar, Ar' = *p*-Tol, *p*-ClC_6H_4), was formed in both cross-experiments ($Ar \neq Ar'$). A mechanism involving 1,2-intramolecular migration of the arylthio group is suggested.

INTRODUCTION

Nucleophilic vinylic substitution reactions have been investigated mainly for substrates containing the leaving group at the β-position to the activating electron-withdrawing group.[1] There are far fewer examples of nucleophilic substitution reactions in vinyl halides which contain activating and leaving groups at one carbon atom,[2] and only in a few studies have these reactions been investigated for systems containing leaving groups at both the α- and β-positions.[3]

In a series of earlier papers, the substitution of α,β-dihalovinyl aryl sulphones was shown to lead to the substitution of only the halogen atom at the β-position.[3c,d] However, later it was found that α,β-dihalovinyl phenyl sulphones **1** react with sodium *p*-thiocresolate with substitution of both halogen atoms, that in the β-position occurring first.[3e] Both mono- (**2**) and disubstituted products were isolated for X = Y = Br, and the retention of configuration on both stages was proved by NMR and x-ray analysis.[3e]



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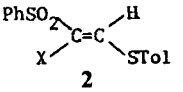

2

X = Br, I;
Y = Cl, Br, I

Vinylic substitution with soft bases such as thiolates is interpreted mostly in terms of an addition–elimination mechanism which includes a nucleophilic attack on the carbon atom bearing the leaving group.[1] Although this reasoning is undoubtedly correct for substitution of the halogen atom at the β-position, it was questioned by us for the substitution at the less activated α-position.[3e] The reason was that the substitution at the α-position proceeds with thiolates but not with alkoxides as nucleophiles, and an alternative mechanism has been suggested.[3e] The aim of this work was to distinguish between different possible mechanisms of vinylic substitution at the less activated α-position, which are shown in Scheme 1.

In path A (α-addition–elimination) the only product formed must be **8**. In path B (β-addition with 1,2-migration of the ArS or Ar'S group) both isomers **8** and **9** should be formed in a ratio which is dependent on the relative migration ability of the corresponding arylthio group. Finally, in path C (with pre-equilibrium β-addition–elimination) one would expect the formation of all possible combinations: two heterosubstituted products **8** and **9** and two homosubstituted products **10** and **11** owing to the presence of both nucleophiles ArS^- and $Ar'S^-$ in the reaction mixture. An ArS/Ar'S exchange in the final products should also be taken into account since it can mask the origin of these species. The use of different nucleophiles, i.e. $ArS^- \neq Ar'S^-$, can also provide an information on the reversibility of the addition step, because the reversibility is the limiting case of the exchange when the nucleophile and the nucleofuge become very similar, up to their identity, but still distinguishable. To discriminate between the mechanisms represented in Scheme 1, the reactions of **1** (X = Y = Br) with two similar nucleophiles *p*-TolSNa and *p*-ClC_6H_4SNa in a different sequence were studied.

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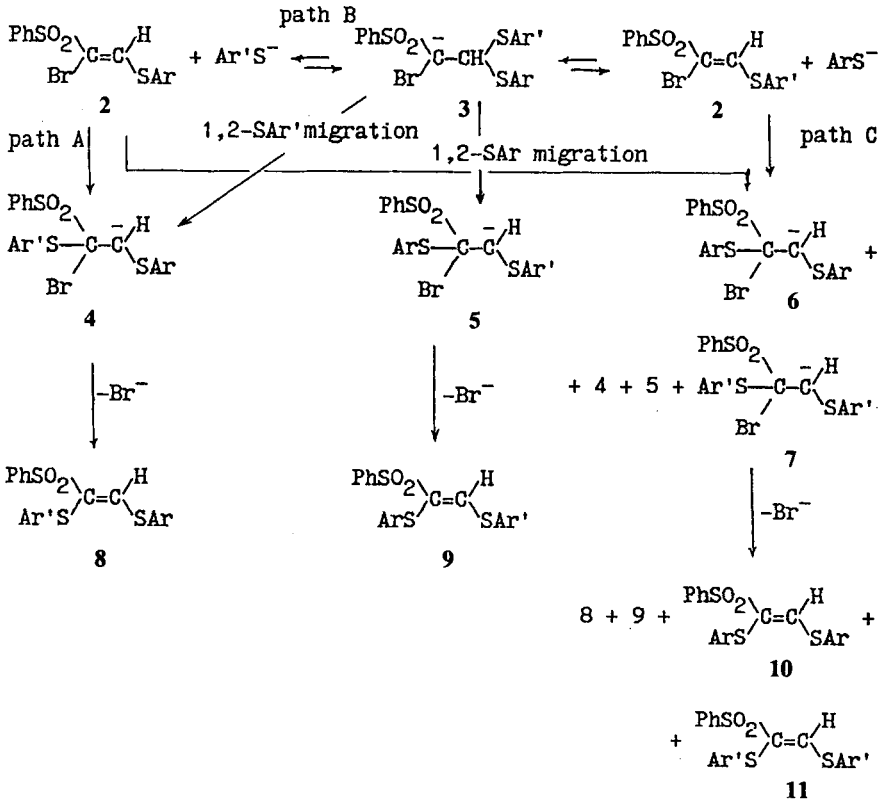


Scheme 1

RESULTS AND DISCUSSION

Monosubstitution products **2** (**a**, Ar = *p*-Tol; **b**, Ar = *p*-ClC_6H_4) were prepared from **1** by its reaction with *p*-TolSNa and *p*-ClC_6H_4SNa, respectively, in methanol. When an equimolar ratio of the substrate and the nucleophile was used virtually pure **2a** was obtained, whereas **2b** turned out to be contaminated with the disubstitution product **11** (hereafter Ar = *p*-Tol; Ar′ = *p*-ClC_6H_4). This implies that the preferability of the *β*- vs *α*-substitution is less pronounced for a weaker base.

Cross-experiments, i.e. **2a** + Ar′S^- and **2b** + ArS^-, were also run. The composition of the reaction mixtures was determined by ^1H NMR spectrometry using the vinylic proton signals at 8·3–8·7 ppm and the methyl protons signals of the ArS group (Table 1).

The reaction of the monosubstitution products **2a** and **2b** with sodium arylthiolates in methanol was carried out by warming the mixture at 50 °C until dissolution took place (5–10 min) and leaving it overnight. Increasing the reaction time or temperature was shown to have no effect on the composition of the reaction mixtures in the cross-experiments. The reaction of **2a** with *p*-ClC_6H_4SNa and that of **2b** with *p*-TolSNa gave mixtures of the four products **8–11** which differed only slightly in their composition.

The **8**:**9**:**10**:**11** ratios were 70:4:12:14 for the reaction of **2a** with *p*-$ClC_6H_4S^-$ and 66:3:13:18 for the reaction of **2b** with *p*-$TolS^-$. The larger proportion

Table 1. Vinylic and methyl proton signals in **1** (δ_{TMS} in DMSO-d_6)

X	Y	δ_H (ppm)	δ_{Me} (ppm)
Br	Br	8·33	—
Br	*p*-TolS	8·36	2·35 (2·34[a])
Br	*p*-ClC_6H_4S	8·45	—
p-TolS	*p*-TolS	8·55	2·34, 2·23 (2·38, 2·28[a])
p-ClC_6H_4S	*p*-ClC_6H_4S	8·71	—
p-ClC_6H_4S	*p*-TolS	8·65	2·355
p-TolS	*p*-ClC_6H_4S	8·62	—[b]

[a] Literature data.[3c]

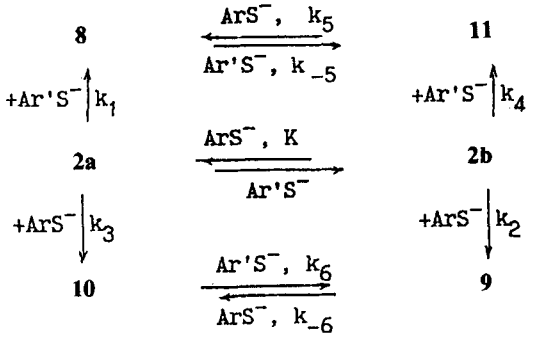
[b] Coincides with the Me signal of the *β*-tolyl group in **10**.

of **11** in the latter case is probably due to its presence as an impurity in the starting **2b**. The H_β signals at 8·55 and 8·71 ppm in the reaction mixture were assigned to products **10** and **11**, respectively, according to their positions in the independently obtained pure samples. Assignment of the H_β signals at 8·65 and 8·62 ppm to isomers **8** and **9**, respectively, was made according to the position and intensity of the methyl protons signals in these species. The most intense signal is that at 2·355 ppm and it belongs to the methyl group of the β-tolylthio group, as it has been shown earlier that the *p*-tolylthio group at the β-position is characterized by a downfield signal of the methyl group compared with that at the α-position.[3e] As the most intense signal of a vinylic proton is that at 8·65 ppm, it has been attributed to product **8**.

To prove the ArS/Ar'S exchange, the reaction of **2b** with *p*-TolSNa was stopped several minutes after mixing, the organic materials were extracted by water–diethyl ether treatment and the water layer was then acidified and extracted with diethyl ether again. Both thiols, *p*-TolSH and *p*-ClC_6H_4SH, were detected in the extract by mass spectrometry. The ArS/Ar'S exchange at the β-position also takes place in the final products **10** and **11**. Thus, when **11** is kept with an equimolar amount of *p*-TolSNa it gives **8**, and the **8** : **11** ratio is 88 : 12, whereas **10** with *p*-ClC_6H_4SNa under the same conditions gives **9** and the **9** : **10** ratio is 16 : 84. It is noteworthy that no exchange of the ArS group at the α-position occurred.

An RS/R'S exchange in vinylic systems has been recently investigated,[4] but both preparative[4a] and kinetic[4b] experiments were run with a large excess of a nucleophile in order to obtain complete conversion[4a] or with the aim of searching for the intermediate in these reactions[4b] rather than investigating the equilibrium between the RS and R'S derivatives.

In order to account for the observed ratios of the products the kinetic model of the process (Scheme 2) was analysed.



Scheme 2

From the model, the following system of equations can be derived:

$$d[\mathbf{8}]/dt = k_1[\mathbf{2a}][Ar'S^-] + k_5[\mathbf{11}][ArS^-] - k_{-5}[\mathbf{8}][Ar'S^-] \quad (1)$$

$$d[\mathbf{9}]/dt = k_2[\mathbf{2b}][ArS^-] + k_6[\mathbf{10}][Ar'S^-] - k_{-6}[\mathbf{9}][ArS^-] \quad (2)$$

$$d[\mathbf{10}]/dt = k_3[\mathbf{2a}][ArS^-] + k_{-6}[\mathbf{9}][ArS^-] - k_6[\mathbf{10}][Ar'S^-] \quad (3)$$

$$d[\mathbf{11}]/dt = k_4[\mathbf{2b}][Ar'S^-] + k_{-5}[\mathbf{8}][Ar'S^-] - k_5[\mathbf{11}][ArS^-] \quad (4)$$

The ratio of the α-ArS to the α-Ar'S derivatives **(9 + 10)/(8 + 11)** is then expressed by the equation

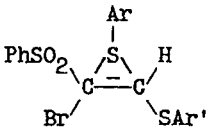
$$(\mathbf{9}+\mathbf{10})/(\mathbf{8}+\mathbf{11}) = (k_2[\mathbf{2b}] + k_3[\mathbf{2a}])[ArS^-]/(k_1[\mathbf{2a}] + k_4[\mathbf{2b}])[Ar'S^-] \quad (5)$$

The $[ArS^-]/[Ar'S^-]$ ratio can be taken from the **8** ⇌ **11** and **10** ⇌ **9** exchange experiments, which give a value of 0·16 ± 0·01. The relationships between the rate constants k_1–k_4 seem to be different in terms of the mechanisms A and C on the one hand and mechanism B on the other. For mechanisms A and C the rate-determining step is the addition of the nucleophile to the double bond. For reactions with different dihalovinyl aryl sulphones the *p*-thiocresolate ion was shown to be *ca* twice as reactive as the *p*-chlorothiophenolate ion.[3e,5] Consequently, we can set $k_3 \approx 2k_1$ and $k_2 \approx 2k_4$. Therefore, for mechanisms A and C the ratio expressed by equation (5) becomes

$$(\mathbf{9}+\mathbf{10})/(\mathbf{8}+\mathbf{11}) = 0{\cdot}32 \quad (6)$$

which is substantially different from the experiment value of 0·19.

On the other hand, for mechanism B the rate-determining step is probably the 1,2-migration of the ArS or Ar'S group. This requires participation of d-orbitals of the sulphur atom in delocalization of the negative charge in the transition state:



and, therefore, the lower reactivity of the *p*-chlorothiophenolate ion in its addition to the double bond can be compensated for by its higher migration ability in the intermediate carbanion **3** (Scheme 1). Hence, to a first approximation, one can assume $k_1 \approx k_2 \approx k_3 \approx k_4$, which yields **(9 + 10)/(8 + 11)** = 0·16 or **(9 + 10)** : **(8 + 11)** = 14 : 86. This almost coincides with the experimental ratio of 16 : 84.

For equal initial concentrations of the reagents, i.e. $[\mathbf{2a}+\mathbf{2b}]_0 = [ArS^- + Ar'S^-]_0 = C_0$, one has

$$[\mathbf{2a}] = [Ar'S^-] = C_0/(1 + K^{1/2}) \quad (7)$$

$$[\mathbf{2b}] = [ArS^-] = C_0K^{1/2}/(1 + K^{1/2}) \quad (8)$$

We can assume that the rate constants for the equilibria in Scheme 2 which involve nucleophilic attack at the C_β atom are much higher than the rate constants k_1–k_4 for the formation of **8**–**11** by nucleophilic attack at the C_α atom. This allows us to apply a steady-state approximation and to simplify equations (1)–(4) to

$$d[\mathbf{8}]/dt = k_1[\mathbf{2a}][Ar'S^-] \quad (9)$$

$$d[\mathbf{9}]/dt = k_2[\mathbf{2b}][ArS^-] \quad (10)$$

$$d[\mathbf{10}]/dt = k_3[\mathbf{2a}][ArS^-] \quad (11)$$

$$d[\mathbf{11}]/dt = k_4[\mathbf{2b}][Ar'S^-] \quad (12)$$

Combining with equations (7) and (8) we obtain the following equation for the ratio of the products:

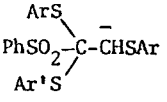
$$\mathbf{8}:\mathbf{9}:\mathbf{10}:\mathbf{11} = k_1 : k_2K : k_3K^{1/2} : k_4K^{1/2} \quad (13)$$

Accepting the above approximation of $k_1 \approx k_2 \approx k_3 \approx k_4$ and assuming $K = 0{\cdot}16^2 = 0{\cdot}026$, we obtain the ratio

$$\mathbf{8}:\mathbf{9}:\mathbf{10}:\mathbf{11} = 74:2:12:12 \quad (14)$$

in excellent agreement with the experimental ratio of 70 : 4 : 12 : 14 for the reaction of **2a** with *p*-$ClC_6H_4S^-$.

Consequently, the experimental data are in better agreement with mechanism B (Scheme 1) which involves an intramolecular 1,2-migration of the ArS or Ar'S group in the intermediate carbanion. This is also proved by the fact that no ArS/Ar'S exchange occurred at the α-position, otherwise the attack of a thiolate ion at the C_α atom would give rise to the carbanion



from which both ArS^- and $Ar'S^-$ could be eliminated.

As this mechanism has been suggested[3e] based on the fact that the substitution at the α-position in **1** takes place with ArS^- but not with MeO^-, it was of interest to study also the reaction of **2** with sodium methoxide. The only product isolated from the reaction of **2a** with MeO^- in methanol turned out to be **10** rather than $PhSO_2C(OMe)=CHSTol\text{-}p$. This is probably the result of exchange of the ArS group at the β-position and the attack of the *p*-$TolS^-$ released at the C_α atom of **2a**. This is consistent with the fact that 1,2-migration of the MeO group is impossible as it requires expansion of the electron shell of the oxygen atom above an octet.[3e]

The idea of 1,2-migration of the nucleophilic group during vinylic substitution has also been proposed by Russell and co-workers for reactions of thiolates and some other soft nucleophiles with 1,1-diphenyl-2,2-dinitroethylene[6] or 1,1-diphenyl-2-nitroethylene[7] and by Benedetti *et al.*[8] to account for the formation of β-mtehoxystyrene from the carbanion $PhCH(OMe)\bar{C}HSO_2R$ (although in the last case, in our opinion, the migration of the phenyl rather than the methoxy group should be considered).

The possible preference of the intramolecular mechanism B over the intermolecular mechanism C is probably due to an entropy effect similar to that responsible for the higher π-nucleophilicity.[9] Carbanions **4** and **5**, although obviously less stable than **3**, have the lone pair on the β-carbon as an 'internal nucleophile' in a close proximity to the C_α reaction centre. This allows the entropy losses to be avoided and also diminishes the energy barrier for the bromide expulsion owing to smaller changes in the interelectronic repulsion[9] on going from **3** to the transition state.

EXPERIMENTAL

Melting points are uncorrected. NMR spectra were taken on Bruker WR 200SY and Bruker AMX 400 instruments in DMSO-d_6. Mass spectra were recorded with a Varian MAT 311 instrument at 70 eV. α,β-Dibromovinyl phenyl sulphone (**1**),[10] α-bromo-β-(*p*-tolylthio)vinyl phenyl sulphone (**2a**)[3e] and α,β-bis(*p*-tolylthio)vinyl phenyl sulphone (**10**)[3e] were prepared earlier. α-Bromo-β-(*p*-chlorophenylthio)vinyl phenyl sulphone (**2b**) was prepared similarly to **2a**,[3e] m.p. 118–119 °C. ^{1}H NMR, δ: 8·45 s (1H, =CH), 7·98 d (2H, *o*-H in Ph), 7·70 m (3H, m, *p*-H in Ph), 7·71 d (2H, *m*-H in ClC_6H_4S), 7·57 d (2H, *o*-H in ClC_6H_4S). ^{13}C NMR, δ: 145·81, 137·13, 134·38, 134·25, 133·02, 132·88, 129·73, 129·71, 129·59, 128·30. MS, *m/z* (relative intensity, %), (ion): 388, 390, 392 (43, 65, 22) (M); 309, 311 (5·6, 2·6) (M-Br); 247, 249, 251 (79, 100, 28) (M – $PhSO_2$); 168, 170 (47, 17) (M – $PhSO_2$-Br); 167, 169 (44, 20) (M – $PhSO_2$ – HBr); 143, 145 (37, 17) (ClC_6H_4S); 141 (9) ($PhSO_2$); 125 (20) (PhSO); 109 (8) (PhS); 77 (59) (Ph). Analysis: calculated for $C_{14}H_{10}BrClO_2S_2$, C 43·15, H 2·59, S 16·45; found, C 43·42, H 2·80, S 16·61%. α,β-Bis(*p*-chlorophenylthio)vinyl phenyl sulphone (**11**) was prepared similarly to **10**,[3e] m.p. 138–139 °C. ^{1}H NMR, δ: 8·72 s (1H, =CH), 7·94 d (2H, *o*-H in Ph), 7·70 d (2H, *m*-H in β-ClC_6H_4S), 7·68 m (1H, *p*-H in Ph), 7·58 m (2H, *m*-H in Ph), 7·58 d (2H, *o*-H in β-ClC_6H_4S), 7·31 d (2H, *m*-H in α-ClC_6H_4S), 7·13 d (2H, *o*-H in α-ClC_6H_4S). ^{13}C NMR, δ: 134·21, 133·84, 132·86, 132·54, 130·20, 129·88, 129·68, 129·48, 129·28, 129·12, 129·05, 128·85, 128·27. MS, *m/z* (%) (ion): 452, 454, 456 (30, 26, 8) (M); 309, 311 (8, 3·5) (M – ClC_6H_4S); 199, 201 (100, 41) (M – $PhSO_2H$ – C_6H_4Cl); 143, 145 (65, 23) (ClC_6H_4S); 141 (11) ($PhSO_2$); 125 (21) (PhSO); 109 (16) (PhS); 77 (51) (Ph). Analysis: calculated for $C_{20}H_{14}Cl_2O_2S_3$, C 52·98, H 3·11, Cl 15·64, S 21·21; found, C 53·11, H 3·18, Cl 15·39, S 21·08%. Compounds **8** and **9** were not isolated but analysed in a mixture with **10** and **11** and are characterized by ^{1}H NMR spectra (Table 1).

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