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STEREOCHEMISTRY AND KINETICS OF THIOPHENOXIDE ION ADDITION TO METHYL *PARA*-SUBSTITUTED PHENYLPROPIOLATE DERIVATIVES IN METHANOL. I

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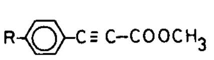
The reactions of a series of methyl *para*-substituted phenylpropiolates with thiophenoxide ion in methanol were studied and their rates measured. Methyl β-thiophenyl esters were obtained as mixtures of *Z* and *E* isomers and their configurations were established by ^{1}H NMR spectroscopy. Good Hammett correlations with ρ values of 1·57–1·97 were obtained, which suggest a carbanionic character of the transition state. A stepwise mechanism proceeding via an intermediate carbanion is postulated for this non-sterospecific addition reaction.

INTRODUCTION

Base-catalysed addition of thiols to activated acetylenes has been thoroughly investigated where only one isomer of the corresponding vinylthio compounds was obtained in most cases according to the rule of *trans* nucleophilic additions,[1-7] although some exceptional cases were also reported.[7-12] Only one study dealing with the use of varying electron demand, in both alkynes and thiols, has been reported.[13] Moreover, the available kinetic data showed that both the thiolate and alkyne molecules are involved in the rate-determining process.[14]

It has been proved that the *Z*/*E* ratio of the products obtained from nucleophilic addition to alkynes is either due to the isomerization under the reaction conditions[8,11] or inherent in the addition, and not a result of postisomerization.[15-17]

The aim of this work was to explore the stereochemistry of the isomer(s) formed from the base-catalysed addition of thiophenol to methyl *para*-substituted phenylpropiolates **1a–e** in methanol as well as studying the kinetics of these reactions to shed some light on the operating mechanism.



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a, R = H; **b**, R = CH_3; **c**, R = Cl; **d**, R = Br; **e**, R = NO_2

RESULTS AND DISCUSSION

The starting materials **1a–e** were prepared as reported previously.[18] The products obtained from the reactions of thiophenoxide ion with the acetylenic esters were isolated and identified as *para*-substituted methyl-β-(thiophenyl)cinnamates, **2a–e**. ^{1}H NMR data indicated the presence of a mixture of *Z* and *E* isomers (Scheme 1).

Configuration of the products

The configuration of the products **2a–e** was assigned by studying their ^{1}H NMR spectra in comparison with those for (*Z*)-methyl *para*-substituted β-(thiophenyl) cinnamates formed by the reaction of thiophenoxide ion with (*Z*)-methyl *para*-substituted β-chlorocinnamates.[19] Further, the theoretical chemical shifts,* obtained by applying the NMR rules of the additivity principle[20,21] for (*Z*)- and (*E*)-β-(thiophenyl)-cinnamate esters were found to be in excellent agreement with the observed values. The ^{1}H NMR spectral data of compounds **2a–e** are given in Table 1. The vinylic and carbomethoxy protons of the *E* isomers were found to appear consistently at higher field than that of the *Z* isomers. This could be attributed to the shielding effect of the thiophenyl and aryl groups which lie in the same side of the double

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*Calculated chemical shifts for the (*Z*)- and (*E*)-methyl *para*-substituted β-thiophenylcinnamates are 6·26 and 5·67 ppm, respectively. No NMR σ values are available for substituted phenyls.

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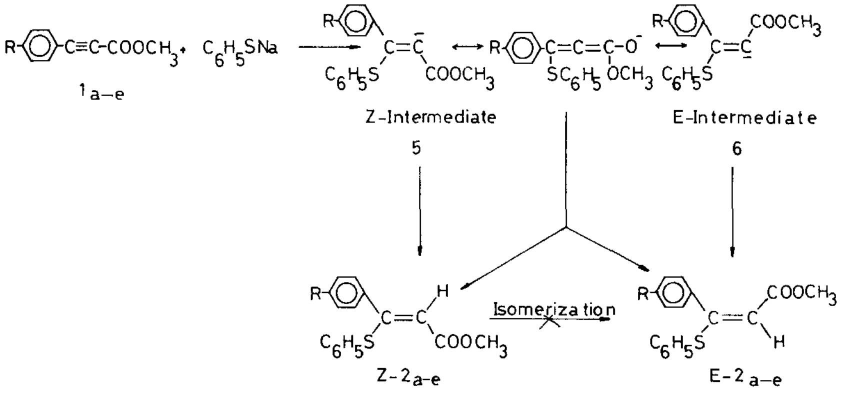

Scheme 1

Table 1. ^{1}H NMR chemical shifts

Compound	R	Aromatic protons	Vinylic protons Z	Vinylic protons E	$-OCH_3$ protons Z	$-OCH_3$ protons E	Z:E ratio
2a	H	7·02–7·30	6·05	5·33	3·75	3·38	73:27
2b	CH_3	6·79–7·40	6·06	5·40	3·69	3·36	80:20
2c	Cl	7·05–7·33	6·00	5·44	3·77	3·42	75:25
2d	Br	7·05–7·43	6·00	5·40	3·76	3·41	75:25
2e	NO_2	6·97–7·43 8·10–7·83	6·33	5·40	3·77	3·43	50:50

bond with the vinylic and carbomethoxy protons, respectively, in case of the *E* isomer.

Kinetic and mechanism

The rates of reactions of **1a–e** with thiophenoxide ion in methanol were measured at different temperatures. The reactions were found to follow second-order kinetics with

$$\text{Rate} = k_2[\mathbf{1a–e}][\bar{S}C_6H_5]$$

measured under pseudo first-order conditions using a 10:1 ratio of **1a–e** to sodium thiophenoxide (see Experimental), where the second-order rate constant $k_2 = k_{obs}/[\mathbf{1a–e}]$. The rate constants ($k_2$) and the derived Arrhenius parameters are given in Table 2. The rates of these reactions and the ratios of the *E* isomer were found to depend on the nature of the *para* substituent, increasing with increase in the electron-withdrawing power of the *para* substituent in the aromatic ring. A Hammett correlation was found to hold well for these reactions (Figure 1). The ρ values range from 1·57 to 1·97, depending on the temperature.

The formation of isomeric mixtures of adducts **2a–e** could be explained on the basis of a stepwise mechanism in which the thiophenoxide ion attacks the β-carbon of the acetylenic ester, giving rise to a configurationally stable *Z* carbanion intermediate **5**, which may undergo either protonation to give a *Z* adduct or isomerization to give the *E* intermediate **6**, which undergoes protonation to give the *E* adduct (Scheme 1). A higher percentage of the *Z* adduct is expected since the *Z* intermediate **5** should suffer less interaction between the negative

Table 2. Specific rate constants[a] and activation parameters for the reactions of **1a–e** with sodium thiophenoxide in methanol

Compound	R	k_2 (l mol^{-1} s^{-1}) 30 °C	40 °C	50 °C	$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$[b] (e.u.)
1a	H	0·12	0·29	0·51	10·97	−25·9
1b	CH_3	0·07	0·16	0·33	13·98	−17·6
1c	Cl	0·49	0·87	1·52	9·78	−27·6
1d	Br	0·49	0·98	1·72	10·28	−25·8
1e	NO_2	4·44	5·98	8·70	5·78	−36·6

[a] $k_2 = k_{obs}/[\mathbf{1a–e}]$. Rate constants were calculated by the least-squares method and the correlation coefficient was 0·99 in most cases. [b] $\Delta S^{\neq} = (4·567 \log k/T) + E_a/T - 49·21$ at 40 °C.

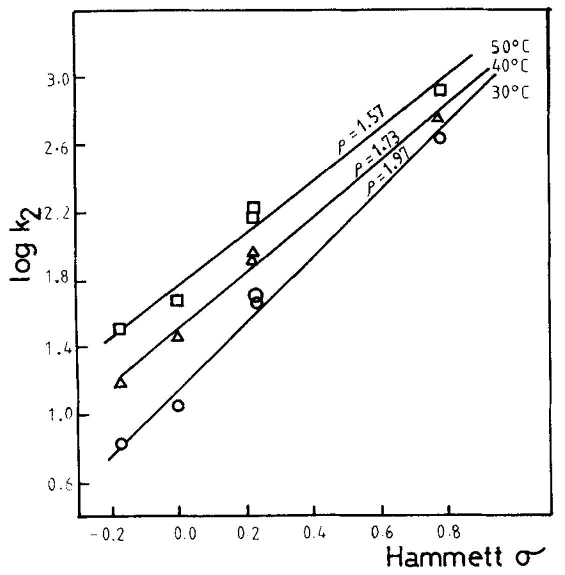

Figure 1. Plot of log k_2 for the reaction of **1a–e** with sodium thiophenoxide against Hammett σ constant

charge and the lone pair of electrons on the sulphur atom.

Certain substituents could conceivably delocalize the charge on the *Z* carbanion intermediate **5**, either partially or completely. Consequently, the electrophilic attack is not expected to be a stereospecific one. This could be clearly observed in case of the *para*-nitro-derivative where a 50:50 *Z*/*E* mixture was obtained. This observation may also indicate an inherent isomerization rather than a post-isomerization. The substantial dependence of the *Z* ratio on the nature of the *para* substituent in the aromatic ring casts doubt on the validity of the concerted mechanism.[9,22] Attempts to effect post-isomerization under different reaction conditions such as shortening the reaction time, utilizing different molar ratios and addition of either thiophenol or base to the isolated mixture of the *E* and *Z* adducts gave unchanged starting materials.

The obtained values of the entropy of activation, $\Delta S^{\neq}$, are comparable to those reported for stepwise mechanisms,[13,23] being less negative than those for concerted ones.[24] Also, the ρ values indicate that considerable anionic character is developed at the carbon atom adjacent to the ester group, and this might lead to the suggestion that a carbanion intermediate is formed.

In conclusion, a stepwise mechanism clearly explains the non-specificity of the addition of sodium thiophenoxide to methyl *para*-substituted phenylpropiolates **1a–e**. Consequently, this type of reaction can be considered as another violation of the rule of *trans*-nucleophilic additions.[1–5]

EXPERIMENTAL

Infrared and ultraviolet spectra were measured on Unicam SP 1025 and 1805 spectrometers, respectively. The ^{1}H NMR spectra were measured at 90 MHz using $CDCl_3$ as solvent and TMS as internal reference. Melting points and boiling points are uncorrected.

Preparation of materials. The synthesis of methyl *para*-substituted phenylpropiolates **1a–e** has been reported previously.[18]

Reaction products. The appropriate arylpropiolate ester (0·01 mol) was dissolved in absolute methanol and a solution of equivalent amounts of sodium and thiophenol (0·01 mol) in absolute methanol was added. The reaction mixture was flushed with nitrogen, thermostated at 40 °C and kept under a nitrogen atmosphere. At the end of the reaction time (as indicated by thin-layer chromatography), the mixture was poured into a large volume of ice-cold water. The precipitate was filtered, washed with 5% sodium hydroxide solution, then crystallized from dilute methanol. The ^{1}H NMR data for the products were found to be the same before and after crystallization (Table 1).

All the following reaction products gave satisfactory elemental analyses. Attempts to separate the *E* and *Z* isomers from each others are in progress. (*E*, *Z*)-Methyl β-thiophenylcinnamate (**2a**), colourless crystals, yield 85%, m.p. 50–57 °C; (*E*, *Z*)-methyl β-thiophenyl-*p*-methylcinnamate (**2b**), colourless plates, yield 80%, m.p. 64–66 °C; (*E*, *Z*)-methyl β-thiophenyl-*p*-chlorocinnamate (**2c**), colourless crystals, yield 92%, m.p. 73–76 °C; (*E*, *Z*)-methyl β-thiophenyl-*p*-bromocinnamate (**2d**), colourless crystals, yield 92%, m.p. 72–77 °C; and (*E*, *Z*)-methyl β-thiophenyl-*p*-nitrocinnamate (**2e**), yellow prisms, yield 95%, m.p. 90–95 °C.

Kinetic measurements. The kinetics of the addition of sodium thiophenoxide to **1a–e** were studied spectrophotometrically using a Pye Unicam SP 800 double-beam recording spectrometer. These reactions were monitored at 310 nm.

The substrate solution (1 ml dissolved in methanol) and sodium thiophenoxide solution (1 ml) (equimolar amounts of thiophenol and sodium metal), which gave final concentrations of $2{\cdot}5 \times 10^{-3}$ M and $2{\cdot}5 \times 10^{-4}$ M, respectively, were transferred into a calibrated flask and the volume was completed to 10 ml with methanol. The reaction mixture was transferred quickly into a well thermostated chamber containing the UV cell. In the reference cell, 2 ml of substrate solution in methanol ($2{\cdot}25 \times 10^{-4}$ M) was placed.

The absorbance A_t at the desired wavelength was recorded at several time intervals. The rate constants of these reactions were calculated under pseudo-first-order conditions using the equation

$$\log(A_\infty - A_t) = \frac{-k_{\mathrm{obs}}}{2\cdot 303}\,t + \log(A_\infty - A_0)$$

where A_0, A_t and A_∞ are the values of the absorbance at zero, time t and infinity, respectively. The values of A_∞ for each kinetic run were taken as the experimentally determined values.

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