Kinetic Study of *E*2 Eliminations from 2-Thienylethyl Bromides and Toluene-*p*-sulphonates promoted by Sodium Ethoxide in Ethanol

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Kinetics of *E*2 elimination from 5-substituted 2-(2-thienyl)ethyl tosylates (ρ 2·23) and bromides (ρ 1·89) and from 2-(3-thienyl)ethyl bromide were studied in EtOH–EtONa at 50°. The transition state for these reactions appeared to be very close to that for the corresponding elimination from 2-phenylethyl derivatives. Values of σ_α (+0·26) and σ_β (−0·05) were calculated for the sulphur heteroatom. No significant conjugative interaction exists between sulphur and the negative charge which develops in the transition state of the reaction.

In *E*2 reactions of alkyl halides, tosylates, and 'onium compounds the presence of a β-phenyl group produces a large increase in the reaction rate.[1] Thus, 2-phenylethyl bromide is 350 fold more reactive than ethyl bromide on treatment with EtO^- in EtOH at 55° and even larger accelerating effects by a β-phenyl ring are observed with charged leaving groups. The phenomenon has been related to the capacity of the phenyl ring to stabilize the incipient negative charge which develops at the β-carbon in the transition state of the *E*2 reaction. This stabilization also occurs by a conjugative mechanism since when substituted phenyl groups are used a correlation with σ^- rather than with σ is found for $-I$, $-R$ substituents.[2]

Whereas elimination reactions in the 2-phenylethyl system have been intensively investigated,[3] corresponding studies on eliminations activated by aromatic systems other than phenyl have not been carried out. Such studies would be of interest since they would furnish quantitative information on the relative capacity of different aromatic rings to stabilize a negative charge. Moreover, the influence of the nature of the aromatic ring on the reaction mechanism, on the structure of the transition state, and on the transmission of substituent effects may be investigated.

On the basis of these considerations we have carried out a kinetic study on eliminations from 5-substituted 2-(2-thienyl)ethyl bromides and tosylates and from

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[1] D. V. Banthorpe, 'Elimination Reactions,' Elsevier, London, 1963, pp. 60, 62.

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[3] W. H. Saunders and A. F. Cockerill, 'Mechanisms of Elimination Reactions,' Wiley, New York, 1973, pp. 60—63.

2-(3-thienyl)ethyl bromide induced by EtONa in EtOH. The effect of the thiophen ring on reactions involving the formation of a positive charge in the transition state has been widely studied.[4] In contrast, less information is available for reactions where a negative charge is involved.

RESULTS AND DISCUSSION

The kinetics of elimination from 2-(5-X-2-thienyl)ethyl bromides and tosylates (X = H, MeO, Me, or Br) and of 2-(3-thienyl)ethyl bromide were studied in EtOH–EtONa, at 50°, by following spectrophotometrically (at the absorption maximum) the formation of vinylthiophen or substituted vinylthiophen. The EtONa concentration (0·1—0·5M) was always in large excess over that of the substrate (*ca.* 10^{-5}M). First-order plots exhibited an excellent linearity up to 90—95% reaction. The yield of olefin was determined spectrophotometrically by using the value of the optical density at infinity (OD_∞) and was found to be independent of the base concentration. This observation and the fact that no olefin was produced from solvolysis of the substrates in EtOH alone clearly show the bimolecular character of the eliminations. Kinetic data obtained at practically the same base concentration (*ca.* 0·44M) are shown in Table 1.

The second-order rate constants k_2^E were found to decrease slightly as the base concentration increased. Some representative data are reported in Table 2. A similar phenomenon has been recently observed for the corresponding elimination from 2-phenylethyl bromide and attributed to the partial dissociation of EtONa into ion pairs.[5] An increase in base concentration leads to a decrease in concentration of the dissociated ions; since the reactivity of these ions is expected to be larger than that of the ion pairs, a decrease of the reaction rate is observed. From a knowledge of the degree of dissociation α of the ion pairs, the observed rate constants may be dissected into the contributions of free ions and ion pairs. If k_i and k_{ip} are the second-order rate constants for attack by free ions and ion pairs, respectively, k_2^E can be expressed in terms of equation (1) and a plot of

$$k_2^E = \alpha k_i + (1 - \alpha)k_{ip} \qquad (1)$$

$k_2^E/(1 - \alpha)$ against $\alpha/(1 - \alpha)$ should be linear, with slope k_i and intercept k_{ip}.

TABLE 1

Kinetic data for elimination from 1-Y-2-(5-X-2-thienyl)-ethane promoted by EtONa in EtOH at 50°

Y	X	[EtONa]/M	Olefin (%) [a]	k_2^E/l mol^{-1} s^{-1} [b]
Br	OCH_3	0·438	85·3	4.03×10^{-3}
	CH_3	0·440	98·3	5.26×10^{-3}
	H	0·453	100·0	9.46×10^{-3}
	Br	0·445	100·0	4.62×10^{-2}
OTs	OCH_3	0·441	35·3	4.26×10^{-4}
	CH_3	0·445	56·4	6.80×10^{-4}
	H	0·449	73·0	1.32×10^{-3}
	Br	0·435	86·2	7.70×10^{-3}

[a] Determined spectrophotometrically. Average of 2—3 determinations for bromides and 6—8 determinations for tosylates. The average error in the olefin yield is <2·5%. [b] The average error in the overall rate constant is 2%. Considering the error in the olefin yield, the k_2^E values should have an uncertainty of *ca.* 5%.

TABLE 2

Influence of base concentration on the second-order rate coefficients for the elimination from 2-(5-methyl-2-thienyl)ethyl tosylate in EtOH–EtONa at 50°

[EtONa]/M	$10^4k_2^E$/l mol^{-1} s^{-1}
0·081	8·04
0·085	7·67
0·249	7·36
0·266	7·09
0·445	6·80

Equation (1) was applied to the kinetics of elimination from the tosylates using the α values determined by Brändström[6] (extrapolated to 50°) and the values of k_i and k_{ip} are reported in Table 3. Treatment of the values of k_i and k_{ip} in terms of the Hammett equation, by using the substituent constants for the thiophen molecule evaluated by Butler,[7] gave fair correlations from which ρ values of $+2.56(\rho_i)$ and $+2.06(\rho_{ip})$ were calculated. Thus, it would seem that the transition state has a larger carbanion character in the reaction with dissociated ions than in the reaction with ion pairs.

TABLE 3

k_i And k_{ip} values (see text) for the elimination from 2-(5-X-2-thienyl)ethyl tosylates in EtOH–EtONa at 50°

X	10^3k_i/l mol^{-1} s^{-1}	10^3k_{ip}/l mol^{-1} s^{-1}
H	2·24	0·97
Br	13·85	5·28
CH_3	1·32	0·40
OCH_3	0·41	0·42

Since dissociated ions are expected to display higher basicity than ion pairs the above result is in agreement with recent findings on the influence of nucleophile basicity on the transition state structure in *E*2 eliminations.[8] Moreover, it is interesting to note that in *syn*-*E*2 reactions of *trans*-2-arylcyclopentyl tosylates more carbanionic transition states are observed for a dissociated base than for the corresponding associated base.[9] Nevertheless, owing to the rather limited range of base concentration investigated (see Experimental section) and to the consequent large errors in the calculations of k_i and k_{ip}, we feel that the above conclusions are, at present, tentative and require further confirmation for different systems.

A point of interest in the present work is the comparison between the ρ values of the 2-(2-thienyl)ethyl and 2-phenylethyl systems. However, in the latter system ρ_i and ρ_{ip} are not known and only a composite

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value of ρ is available. For comparative purposes ρ values for the reactions of 2-(2-thienyl)ethyl tosylates and bromides were therefore calculated from k_2^E values at the same base concentration. Clearly, this procedure, which has been used by several workers[10] to overcome the difficulties related to the dependence of k_2^E values on the base concentration, is not entirely correct since the reactions induced by free ions and ions pairs can have, as previously shown, different selectivity. Nevertheless, the use of composite values of ρ may be sufficiently justified in a qualitative discussion not involving a precise interpretation of small differences in the ρ values.

Using k_2^E data reported in Table 1, ρ values of +2·23 (r 0·996, s 0·061) and +1·89 (r 0·990, s 0·081) were calculated for the elimination reactions of 2-(2-thienyl)-ethyl tosylates and bromides, respectively. These values are practically identical with those reported for the corresponding eliminations from 2-phenylethyl tosylates (ρ +2·27)[11] and bromides (ρ +1·93).* Thus, it is clear that when 2-(2-thienyl) is substituted for 2-phenyl in the ethyl system the transition state structure remains practically unchanged. Further evidence on this point is given by the relative reaction rates of tosylates and bromides (k_{OTs}/k_{Br}) which can be taken as indicative of the extent of C_α–leaving group bond breaking in the transition state.[12] The k_{OTs}/k_{Br} value is 7·2 for the 2-(2-thienyl)ethyl system and 5·7 for the 2-phenylethyl group. Thus, a similar degree of C_α–leaving group bond breaking in the transition state for the two systems may be predicted.

On comparing the elimination rates of 2-(2-thienyl)-ethyl and 2-(3-thienyl)ethyl bromide with that of ethyl bromide,[13] it is observed that a 2-thienyl group in the β-position increases the rate by a factor of *ca.* 1000. For the 3-thienyl group a rate increase by a factor of 150 is observed. Thus, the 2-thienyl group exerts a larger kinetic effect on the elimination rate than the 3-thienyl group, as expected since in the 2-(2-thienyl)-ethyl system the reaction centre is nearer to the sulphur atom. Relative to a phenyl group the accelerating effect is slightly larger in the case of 2-thienyl and slightly smaller for 3-thienyl. Differences are, however, small and it may be concluded that the capacity of a thienyl group to stabilize a negative charge which develops in a side-chain is similar to that of a phenyl group.

The effect of five-membered heteroaromatic systems on rates and equilibria may also be discussed by considering the heteroatom as a substituent which replaces a –CH=CH– group in benzene.[14] This approach allows the effect of the heteroatom (in reaction involving the α- and β-positions of the ring) to be expressed in terms of substituent constants σ_α and σ_β.

In our case a σ_α value of +0·26 for the –S– group is calculated from the equation $\log k/k_0 = \rho\sigma_\alpha$ where k_0 is the rate constant for the elimination reactions of 2-(2-thienyl)ethyl bromide and 2-phenylethyl bromide,[2] respectively, and ρ is the reaction constant for the eliminations from 2-phenylethyl bromides. In the same way a σ_β value of −0·05 is obtained for the heteroatom from the kinetic data for the elimination reaction of 2-(3-thienyl)ethyl bromide.

These values of σ_α and σ_β are in agreement with those calculated (σ_α 0·3, σ_β <0·1) from the base catalysed hydrogen exchange of 2- and 3-methylthiophen,[15] a reaction which should be characterized by a transition state in some respects, similar to that of the elimination reaction.

Interestingly, the σ values for the sulphur atom calculated from the elimination rates are similar to the values of σ^0 [15] and σ^* [16] which should measure resonance independent polar effects of the heteroatom. This finding shows that in the elimination reaction of 2-thienylethyl derivatives no significant conjugative interaction occurs between the heteroatom and the partial negative charge which develops in the transition state.

EXPERIMENTAL

Materials.—2-(2-*Thienyl*)*ethyl bromide*. To a solution of 2-(2-thienyl)ethanol[17] (7·4 g, 0·058 mol) in dry benzene (10 ml) was added dropwise, with cooling and stirring, PBr_3 (12·2 g) in dry benzene (7 ml). The mixture was left for 0·5 h in a steam-bath. After cooling, water (35 ml) was added and the organic layer was separated, washed, and dried. 2-(2-Thienyl)ethyl bromide (4·1 g, 0·021 mol) was obtained by distillation, b.p. 100—102° at 15 mmHg (lit.,[18] 98—99° at 13 mmHg).

2-(5-*Bromo*-2-*thienyl*)*ethyl bromide*. To 2,5-dibromothiophen[19] (0·2 mol) in anhydrous ether (100 ml) were added, at −70° under nitrogen, n-butyl-lithium (0·2 mol) in hexane and successively ethylene oxide (0·4 mol) in anhydrous ether. The mixture was allowed to warm to room temperature, poured into ice–water, and the organic layer was extracted with n-pentane. After drying (Na_2SO_4), the solvent was removed. Distillation of the residue gave 2-(5-bromo-2-thienyl)ethanol (25·2 g, 0·12 mol), b.p. 99—100° at 0·6 mmHg (Found: C, 34·95; H, 3·45. Calc. for C_6H_7BrOS: C, 34·8; H, 3·4%). The alcohol (0·1 mol) was converted by the procedure above to 2-(5-bromo-2-thienyl)-ethyl bromide (0·046 mol), b.p. 92—93° at 0·05 mmHg, τ ($CDCl_3$) 6·67 (2H, d, H_2C_β), 6·47 (2H, d, H_2C_α), and 3·34

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* Calculated from kinetic data at 50° reported in ref. 2. A value of +2·14 is reported in ref. 11.

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and 3·03 (2H, dd, thienyl H) (Found: C, 26·65; H, 2·25. Calc. for C_6H_6BrS: C, 26·65; H, 2·2%).

2-(5-*Methyl*-2-*thienyl*)*ethyl bromide*. This was prepared from 2-(5-methyl-2-thienyl) ethanol [20] using the procedure above, b.p. 69—70° at 0·2 mmHg, τ ($CDCl_3$) 7·53 (3H, t, CH_3), 6·61 (4H, m, H_2C_β and H_2C_α), and 3·34 (2H, s, thienyl H) (Found: C, 41·05; H, 4·4. Calc. for C_7H_9BrS: C, 41·0; H, 4·4%).

2-(5-*Methoxy*-2-*thienyl*)*ethyl bromide*. 2-(5-Methoxy-2-thienyl)ethanol was prepared from 5-methoxy-2-bromothiophen [21] by the procedure described for 2-(5-bromo-2-thienyl)ethanol, b.p. 97° at 0·6 mmHg (Found: C, 52·95; H, 6·15. Calc. for $C_7H_{10}O_2S$: C, 53·15; H, 6·35%). The alcohol was converted into the corresponding tosylate [22] which was reacted with anhydrous lithium bromide in dry acetone at room temperature for 72 h.[23] The oil obtained was purified by column chromatography on deactivated silica gel, τ (CCl_4) 6·73 (4H, m, H_2C_β and H_2C_α), 6·19 (3H, s, OCH_3), and 4·03 and 3·57 (2H, dd, thienyl H) (Found: C, 37·75; H, 4·15. Calc. for C_7H_9BrOS: C, 38·0; H, 4·05%).

2-(3-*Thienyl*)*ethyl bromide*. 2-(3-Thienyl)ethanol [24] was converted into the corresponding bromide using the procedure described. The bromide was found to contain *ca*. 3% of 2-(2-thienyl)ethyl bromide and was purified by preparative g.l.c., b.p. 55—56° at 0·4 mmHg, τ ($CDCl_3$) 7·0—6·34 (4H, m, H_2C_β and H_2C_α) and 3·24—2·65 (3H, m, thienyl H) (Found: C, 38·55; H, 3·95. Calc. for C_6H_7BrS: C, 37·7; H, 3·65%).

2-(5-X-2-*Thienyl*)*ethyl tosylates*. All these compounds were prepared from the corresponding alcohols by using the general procedure described by Tipson: [22] 2-(2-thienyl)ethyl tosylate, m.p. 33—34° (lit.,[4] 32·5—33·5° (Found: C, 55·5; H, 4·8. Calc. for $C_{13}H_{14}O_3S_2$: C, 55·3; H, 4·95%); 2-(5-bromo-2-thienyl)ethyl tosylate, m.p. 54·5—55·5° (lit.,[4] 52·8—53·8°) (Found: C, 42·75; H, 3·8. Calc. for $C_{13}H_{13}BrO_3S_2$: C, 43·2; H, 3·6%); 2-(5-methyl-2-thienyl)-ethyl tosylate, m.p. 33·5—34·5° (lit.,[4] 35·5—36·5°) (Found: C, 56·7; H, 5·2. Calc. for $C_{14}H_{16}O_3S_2$: C, 56·75; H, 5·4%); 2-(5-*methoxy*-2-*thienyl*)*ethyl tosylate*, τ ($CDCl_3$) 7·67 (3H, s, CH_3), 7·10 (2H, t, H_2C_β), 6·63 (3H, s, OCH_3), 5·93 (2H, t, H_2C_α), 4·06 and 3·64 (2H, dd, thienyl H), and 2·77 and 2·33 (4H, dd, C_6H_4) (Found: C, 53·85; H, 5·25. $C_{14}H_{16}O_4S_2$ requires C, 53·85; H, 5·15%).

Ethanol was purified [25] and carefully fractionated with a Todd column.

Products.—All the olefins, with the exception of 3-vinylthiophen, were obtained by the reaction of the tosylates with EtO^- in EtOH. The products were purified by column chromatography on deactivated silica gel. In most cases the substitution products were also obtained: 2-vinylthiophen, $\lambda_{max.}$ (EtOH) 274 nm (ε 1·08 × 10^4) [lit.,[26] 274 nm (1·06 × 10^4)]; 2-thienylethyl ethyl ether, τ ($CDCl_3$) 8·79 (3H, t, CH_3), 6·93 (2H, t, H_2C_β), 6·77—6·27 (4H, m, H_2C_α and OCH_2), and 3·24—2·87 (3H, m, thienyl H); 5-*bromo*-2-*vinylthiophen*, $\lambda_{max.}$ (EtOH) 287 nm (ε 1·38 × 10^4), τ ($CDCl_3$) 4·88 and 4·57 (2H, dd, H_2C_β) and 3·56—3·05 (3H, m, thienyl H and HC_α) (Found: C, 38·2; H, 2·7. C_6H_6BrS requires C, 38·1; H, 2·65%); 5-methyl-2-vinylthiophen, $\lambda_{max.}$ (EtOH) 284 nm (ε 1·27 × 10^4), τ ($CDCl_3$) 7·61 (3H, s, CH_3), 5·79 (2H, m, H_2C_β), 4·50 (1H, m, HC_α), and 3·44 and 3·25 (2H, dd, thienyl H); 2-(5-*methyl*-2-*thienyl*)*ethyl ethyl ether*, τ ($CDCl_3$) 8·82 (3H, t, CH_3), 7·58 (3H, s, CH_3), 7·00 (2H, t, H_2C_β), 6·62—6·30 (4H, m, H_2C_α and OCH_2), and 3·56—3·37 (2H, m, thienyl H) (Found: C, 64·1; H, 8·35. $C_9H_{14}OS$ requires C, 63·55; H, 8·25%); 5-methoxy-2-vinylthiophen, $\lambda_{max.}$ (EtOH) 296 nm (ε 1·42 × 10^4), τ ($CDCl_3$) 6·12 (3H, s, $-OCH_3$), 5·05 and 4·73 (2H, dd, H_2C_β), 3·93 and 3·42 (2H, dd, thienyl H), and 3·58—3·09 (1H, m, HC_α); 2-(5-*methoxy*-2-*thienyl*)*ethyl ethyl ether*, τ ($CDCl_3$) 6·78 (3H, t, CH_3), 7·07 (2H, t, H_2C_β), 6·72—6·22 (4H, m, H_2C_α and OCH_2), 6·19 (3H, s, OCH_3), and 3·98 and 3·54 (2H, dd, thienyl H) (Found: C, 58·25; H, 7·3. $C_9H_{14}O_2S$ requires C, 58·05; H, 7·55%). 3-Vinylthiophen was prepared as described by Troyanowski,[27] b.p. 60—61° at 30 mmHg (lit.,[27] 48—51° at 19·5 mmHg), $\lambda_{max.}$ (EtOH) 244 nm (ε 1·18 × 10^4).

Kinetics.—For all compounds, the appearance of 3- and 2-vinylthiophen or 5-substituted-2-vinylthiophen was followed spectrophotometrically. Kinetics were carried out in a stoppered two-limb silica cell. In one limb was placed base solution (1 ml) and in the other substrate solution (1 ml). The cell was placed in the thermostatted compartment of a Beckman DB-GT spectrophotometer. After *ca*. 0·5 h the solutions were mixed thoroughly and the cell rapidly placed again in the cell compartment of the spectrophotometer. A large excess of base (at least 500-fold) was used in each case and first-order rate constants were determined from the slope of the plot of log ($OD_\infty - OD_t$) against time, where OD_t is the absorbance at time t and OD_∞ the absorbance at infinity (at least 10 half-times). When the EtONa concentration was >0·5M some difficulty was experienced in obtaining a constant value of OD_∞. Second-order rate constants k_2 were obtained by dividing the first-order rate constants by the base concentration. The product k_2 × % olefin gave the second-order rate constants k_2^E.

Thanks are due to the C.N.R. for support.

[4/2134 *Received*, 15*th October*, 1974]

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