Gas-phase pyrolysis of thiopheneacetic acids, thienylethanols, and related compounds — protophilicity of ring π -electrons and relative acidities of hydrogen-bond donors of hydroxyl groups

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Abstract: Based on kinetic data of thermal gas-phase elimination reactions, the following Arrhenius log A (s⁻¹) and E_a (kJ mol⁻¹) values, respectively, are obtained: 10.76 and 153.5 for 3-thiopheneacetic acid (1), 10.08 and 149.4 for 2-thiopheneacetic acid (2), 12.04 and 207.1 for 2-(3-thienyl)ethanol (3), 11.55 and 203.3 for 2-(2-thienyl)ethanol (4), 10.91 and 123.4 for 2-thiopheneglyoxylic acid (5), 11.05 and 223.8 for 1-(2-thienyl)propan-1-one (6), and 10.33 and 149.8 for 3-thiophenemalonic acid (7). The products of these pyrolytic reactions were either carbon dioxide or formal-dehyde in addition to methylthiophene or thiophenecarboxaldehyde. Both positional and molecular reactivities of the substrates and related compounds are compared, and the results are rationalized on the basis of a reaction pathway involving a concerted six-membered transition state.

Key words: thiophenes, gas-phase, pyrolysis, kinetics, mechanism.

Résumé : Sur la base de données cinétiques de réactions d'élimination thermiques en phase gazeuse, on a déterminé les valeurs suivantes d'Arrhenius suivantes log A (s⁻¹) et E_a (kJ mol⁻¹) pour respectivement l'acide 3-thiophèneacétique (1, 10,76 et 153,5), l'acide 2-thiophèneacétique (2, 10,08 et 149,4), le 2-(thién-3-yl)éthanol (3, 12,04 et 207,1), le 2-(thién-2-yl)éthanol (4, 11,55 et 203,3), l'acide 2-thiophèneglyoxylique (5, 10,91 et 123,4), la 1-(thién-2-yl)propan-1-one (6, 11,05 et 223,8) et l'acide 3-thiophènemalonique (7, 10,33 et 149,8). Les produits de ces réactions de pyrolyse sont le bioxyde de carbone ou le formaldéhyde ainsi que le méthylthiophène ou le thiophènecarboxaldéhyde. On a comparé les réactivités positionnelles ainsi que moléculaires des substrats examinés ici ainsi que celles de composés apparentés et on rationalise les résultats en se basant sur une voie réactionnelle impliquant un état de transition concerté à six chaînons.

Mots clés : thiophènes, phase gazeuse, pyrolyse, cinétique, mécanisme.

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Introduction

Thiophene is classified as an electron-rich (π -excessive) heteroaromatic compound, with its aromaticity between that of furan and benzene, and reactivity towards electrophiles ca. 10³- to 10⁵-fold higher relative to benzene (1, 2). The structural effects associated with the 2,3-conjugative interaction and the high 2:3-bond order superimposed upon an intrinsic 2 > 3 positional reactivity serve to explain the relative rates and partial rate factors obtained in electrophilic aromatic substitution reactions of thiophene and its N, O, and Se analogues and monosubstituted derivatives (3–5). Hammett substituent-replacement constants reported for both solution

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and gas-phase reactions suggest that the 2- and 3-thienyl ring systems act as electron withdrawing and electron donating groups, respectively (6). An electron withdrawing effect would be expected to augment the electrophilic nature of the hydroxyl hydrogen of both the alcohol and carboxylic acid moieties of substituted thiophenes. The present study involves thiophenes substituted at the 2- and 3-positions with groups in which terminal O-H moieties serve as H-bond donor acids, and where a protonic hydrogen is available for intramolecular electrophilic H-exchange processes. Reactions of this nature, for which a concerted six-membered transition state (TS) is postulated, are expected to have favourable conformations and effective intramolecular pre-organization. A representative example is the thermal gas-phase elimination reaction of 2-thiopheneglyoxylic acid, the final product of which is 2-thiophenecarboxaldehyde (Scheme 1).

Previous studies on comparable reactions have lead to the conclusion that, during the development of the TS of the elimination process, either bond **a**, **b**, or **d** (Scheme 1) could be effectively displaced further away from the reacting site compared with the other two bonds, or that a combined

Scheme 1. Reaction pathway, concerted six-membered TS, and final product of thermal gas-phase elimination.



effect on the observed reactivity involves either two or all three of the bonds (7–11). The effect of the double bond (**a**) is associated with the lability (protophilicity) of its π -electrons, the effect of **b** depends on bond polarity, and that of **d** results from the relative acidity of the H-bond donor and the magnitude of the positive charge developing on the hydrogen. In addition, an important factor in these elimination reactions is the relative thermodynamic stability of the incipient moieties leading to the products (10*a*, *c*). It is noteworthy that a six-membered TS has also been proposed for decarboxylation reactions of heteroarylacetic acids in aqueous media (12).

Results and discussion

Kinetics

The kinetic data of the gas-phase elimination reactions of the seven compounds (1-7) under study are given in Table 1. Each rate constant represents an average from a set of three values obtained in three separate kinetic runs; all three values were measured at the same temperature. The agreement between the rate-constant values in each set is within $\pm 2\%$. Each elimination process was monitored until 90-95% of reaction was completed. The temperature range $(54 \pm 7 \text{ K})$ over which each compound was investigated is a prerequisite for reliable kinetic studies (9-11). Arrhenius parameters were obtained using the results from Table 1. The Arrhenius plots were linear over the temperature range studied, with correlation coefficients of the order of 0.990 ± 0.009 . For example, for 3-thiopheneacetic acid (1) at 53.5 K the correlation coefficient is 0.9994. Arrhenius log A (s⁻¹), $\Delta S^{\#}$ (J mol⁻¹ K⁻¹), the energy of activation (E_a , kJ mol⁻¹), and the first-order rate constants (k, s^{-1}) of the elimination reactions at 600 K are recorded in Table 2. The values of $\log A$ (s⁻¹) show a narrow range for each set of compounds (10.5 ± 0.4) for the acids and 11.8 \pm 0.2 for the alcohols), but a wider range for the E_a (kJ mol⁻¹) values, an indication of dependence of the reaction on $E_{\rm a}$. This seems to be a common feature of polar thermal gas-phase elimination processes (13). The values for $\Delta S^{\#}$ (J mol⁻¹ K⁻¹) are negative and relatively large, which might be the result of considerable pre-organization leading to the formation of the six-membered TS postulated for such gas-phase reaction pathways (7). It is to be noted that an earlier but independent preliminary study by our group on the present substrates gave almost identical reaction rate factors at 450 K; however, only the rates for pyrolysis at 600 K are reported here.

Reaction products

Reaction products for complete pyrolysis were obtained for all substrates except 1-(2-thienyl)-1-propanone, since its complete pyrolysis required temperatures beyond the operating temperatures of the reactors. Pyrolyses were carried out either in a flow reactor or in a sealed-tube pyrolyzer at tem-

Table 1. Kinetic data for pyrolysis of compounds 1–7.

Compd.	T (K)	$k \times 10^4 ({ m s}^{-1})$	Compd.	<i>T</i> (K)	$k \times 10^4 ({ m s}^{-1})$
1	564.3	3.303	5	443.4	1.574
	574.2	6.171		453.5	4.747
	584.1	9.986		463.5	12.25
	588.8	15.13		473.2	23.47
	593.8	22.74		477.2	25.59
	603.4	28.43		483.4	41.20
	613.0	45.07		493.0	68.35
	617.8	50.98		503.1	83.67
2	563.2	1.795	6	774.9	0.894
	573.3	2.627		785.1	1.748
	583.8	5.749		795.2	2.506
	593.4	8.984		805.5	3.853
	603.4	13.31		813.4	4.755
	613.2	20.07		821.9	4.932
	623.4	31.63			
3	684.8	1.574	7	563.3	2.069
	695.1	3.229		573.8	5.866
	705.1	5.149		583.7	8.515
	715.3	7.390		594.6	15.00
	720.8	11.78		599.0	18.82
	725.2	16.64		604.4	25.24
	735.3	20.75		613.9	37.30
	745.6	32.85			
4	704.5	3.003			
	714.9	4.191			
	725.1	9.145			
	735.2	9.865			
	745.2	17.66			
	755.4	31.49			
	765.3	45.79			

peratures comparable with those used in the kinetic investigations. The reactions were allowed ample residence time to ensure maximum pyrolysis. The constituents of the pyrolysates were analyzed using GC-MS, FT-IR, and ¹H NMR techniques. Conversion of the acid and alcohol starting materials into reaction products was monitored in part by observing the absence of the characteristic FT-IR absorption peaks of the substrates. Pyrolysis of 2-thiopheneacetic acid (2) and 2-(2-thienyl)ethanol (4) gave 2-methylthiophene $(m/z; M^{\bullet+} = 98$ and base peak at 97; the corresponding values for their precursor substrates are $M^{\bullet+} = 142$ and $M^{\bullet+} =$ 128, respectively). On the other hand, pyrolysis of 3thiopheneacetic acid (1) and 2-(3-thieny)ethanol (3) produced 3-methylthiophene with m/z values identical to those of their 2-substituted analogues. Differentiation between 2methylthiophene and 3-methylthiophene was derived from their respective ¹H NMR spectra (2-methylthiophene (CDCl₃) δ: 3.2-3.5 (s, 3H, CH₃), 6.8-7.7 (m, 3H, HAr); 3methylthiophene (CDCl₃) δ: 2.1-2.3 (s, 3H, CH₃), 6.9-7.5 (m, 3H, HAr)). Pyrolysis of 2-thiopheneglyoxylic acid (5) gave 2-thiophenecarboxaldehyde (m/z: $M^{\bullet+} = 112$, and fragment ions at 111 and 83; v_{max} : 1655 (C=O); and δ (CDCl₃): 7.3-8.3 (m, 3H, HAr), 10.0 (s, 1H, HCO)). It is noteworthy

Compd.	<i>Т</i> (К)	$\begin{array}{c} E_{\rm a} \\ (\rm kJ \ mol^{-1}) \end{array}$	$\log A$ (s ⁻¹)	$\Delta S^{\#}$ (J mol ⁻¹ K ⁻¹)	Corr. Coeff.	k (s ⁻¹)
1	53.5	153.5	10.76	-44.8	0.9994	2.51×10^{-3}
2	60.2	149.4	10.08	-57.7	0.9866	1.20×10^{-3}
3	60.8	207.1	12.04	-20.3	0.9943	1.03×10^{-6}
4	60.8	203.3	11.55	-29.6	0.9906	7.08×10^{-7}
5	59.7	123.4	10.91	-41.8	0.9918	1.48
6	47.0	223.8	11.05.	-39.2	0.9814	3.72×10^{-9}
7	50.6	149.8	10.33	-53.0	0.9827	1.95×10^{-3}

Table 2. Arrhenius parameters and rate coefficients (k, s^{-1}) at 600 K and $\Delta S^{\#}$ values for pyrolysis of compounds 1–7.

Scheme 2. Concerted four-membered TS (a) and six-membered TS (b) for pyrolysis of 3-thiopheneacetic acid.



that 3-thiophenemalonic acid (7) gave pyrolysis products and a rate constant similar to those of 3-thiopheneacetic acid, an indication that the latter seems to be the primary decomposition product, which then pyrolyzes further into 2methylthiophene and CO_2 .

Reaction pathway and molecular reactivity

The present results for substrates 1–7 suggest a homogeneous unimolecular first-order elimination process. Moreover, the magnitudes of the Arrhenius-parameter values are in the range expected for such reactions (7, 13–16). The homogeneous nature and the lack of reactor-surface effects were proven by increasing the available surface area for reaction using tubes packed with glass helices. An increase of ca. 50% in surface area produced no noticeable change in the reaction rates. Kinetic runs were also conducted in the presence and absence of cyclohexene (free-radical scavenger). The rates, however, remained the same within experimental error. Additional analysis of the pyrolysates gave no indication of a radical-based reaction product.

Product formation can be rationalized either (i) on the basis of a mechanism involving a concerted four-membered TS or (ii) by a pathway with a concerted six-membered TS. The two mechanisms are shown in Scheme 2 for the gas-phase elimination reaction of 3-thiopheneacetic acid.

Although it is much simpler to explain product formation using the four-membered TS mechanism (Scheme 2a), theoretical and experimental evidence favour the six-membered TS (Scheme 2b). This evidence includes the following: (*i*) the conformation of the cyclic six-membered structure is known to be much more stable compared with the highly strained four-membered counterpart. (*ii*) The development of the six-membered TS requires a more facile intramolecular transfer of the electrophilic hydrogen to the protophilic thiophene ring positions, which are amenable to electrophilic **Scheme 3.** Calculated reaction mechanism for thermal gas-phase elimination of diacetamide.

attack. (*iii*) Theoretical ab initio calculations on the mechanism of similar thermal gas-phase elimination reactions gave results based on a six-membered TS that agree well with experimental values. In addition, these calculations have replaced the proposed four- and five-membered TS with fiveand six-membered structures, respectively (17, 18).

The theoretical studies used analytical gradients at the MP2//RHF/6-31G* level of theory, optimization routines, and microcanonical probability fluxes through TS to map PES and to calculate activation barriers and rate constants for the thermal reactions. The compounds whose elimination reactions were assigned a concerted six-membered TS include diacetamide, β-hydroxyketones, acetic anhydride, and methyl benzoylformate (17). Concerted five-membered TS were calculated for the pyrolysis of pyruvic acid, benzoyl formic acid, 3-hydroxy-3-methyl-2-butanone (α-oxoacids and α -hydroxyketone), and a large number of α -substituted carboxylic acids (17, 18). The theoretical calculations further confirm that the development of the TS involves intramolecular hydrogen transfer to a protophilic site and concomitant formation and breaking of the other bonds in the concerted structure. Typically, the reaction pathway calculated for the thermal gas-phase elimination reaction of diacetamide shown in Scheme 3 reproduces the cyclic sixmembered TS, which accounts for the kinetic values and the reaction products reported in the experimental study of this substrate (17*a*, 19).

The six-membered TS mechanism (Scheme 2*b*), presently adopted to account for the kinetic results and reaction products of the thiophene compounds (1–7), has also been proposed for the thermal elimination reaction of 3-butenoic acid (8), 3-buten-1-ol (9), and the π -deficient 2-(2-ethoxy)pyridine systems (7, 15). The values of the Arrhenius parameters reported for the latter systems are comparable to those obtained in the present study.

The gas-phase molecular and positional reactivities of the thiophene compounds (1-7) and related systems (8-10) given in Scheme 4 allow for the following comparisons to be made:

(*i*) the thiopheneacetic acids **1**, **2** are more reactive than their thienylethanol analogues (**3**, **4**) by a factor ca. 2×10^3 .

Scheme 4. Rate coefficients (k, s^{-1}) at 600 K and selected rate ratios for pyrolysis of present substrates (1–7) and related compounds (8–10).



This large difference in molecular reactivity is ascribed to a more acidic H-bond (bond **d**, Scheme 1) and to the magnitude of the positive charge developing on the incipient hydrogen of the OH group of substrates 1, 2. The difference in reactivity becomes much larger (a factor of 4×10^8) when the O–H moiety of 5 is compared with a C–H bond of related ketone 6.

(*ii*) 2-Thiopheneglyoxylic acid (**5**) is 1.2×10^3 more reactive than 2-thiopheneacetic acid (**2**). This is a consequence of the effect of the relative bond polarity (bond **b**, Scheme 1) on molecular reactivity, and on the repulsion between the positive charge on the carbon atoms of the adjacent carbonyl groups of **2**, which result in a more polar bond (**b**) in **2**.

(*iii*) Aliphatic 3-butenoic acid (8) and 3-buten-1-ol (9) are both more reactive than their heteroaromatic thienyl counterparts (3- and 2-thiopheneaceatic acid (1, 2) and 1-(3thienyl)- and 1-(2-thienyl)ethanol (3, 4), respectively). The rate factors involved are, respectively, 18 and 37 for the former, and 244 and 355 for the latter pair of analogues. This pattern of relative reactivities indicates that although the thiophene ring is π -excessive in nature, its π bonds (bond **a**, Scheme 1) are still less protophilic than the aliphatic π bonds. Comparative protophilicity of bond **a** also explains why the rate of the elimination reaction of 3-buten-1-ol (k = 2.5×10^{-4} s⁻¹ at 600 K, protophilic alkene π bond) is much lower than that of 4-hydroxy-2-butanone ($k = 1.5 \times 10^{-2}$ s⁻¹ at 600 K, protophilic carbonyl moiety) (15). The effect of aromaticity on molecular reactivity is demonstrated when thiopheneglyoxylic acid (5) is shown to be twofold more reactive than benzoylformic acid (10); the latter being the more aromatic in nature (20).

(*iv*) 3-Thiopheneacetic acid (1) is more reactive than its 2isomer (2) by a factor of ca. 2, whereas the corresponding relative rate factor for the thienylethanols (3 and 4) is 1.5. These rate factors, though moderate, are nevertheless consistent with the accepted intrinsic 2 > 3 positional reactivities of π -excessive five-membered aromatic heterocycles (4, 5). In the present systems, the protonic H of the group at the 3position is reacting with the more protophilic π -bond at the nuclear 2-position.

(v) 3-Thiophenemalonic acid (7) has two equivalent carboxylic acid groups that are equally susceptible to decarboxylation during pyrolysis, whereas 3-thiopheneacetic acid (1) only has one such group. Statistically, 7 would be expected to be twice as reactive as 1; however, the rate constants of the elimination reaction of the two acids are comparable $(2.0 \times 10^{-3} \text{ s}^{-1} \text{ and } 2.5 \times 10^{-3} \text{ s}^{-1}$, respectively). The reason that the higher reactivity expected for 7 is not observed might be due to intramolecular H-bonding involving the two acid groups, with an adverse effect on the molecular reactivity of acid 7.

Experimental

Materials, techniques, and instrumentation

The acids, alcohols, and ketone (1-7) under investigation are commercially available from Aldrich. The substrates and the constituents of their pyrolysates were characterized using GC–MS, FT-IR, and ¹H NMR spectroscopy. Instrumentation included a Finnigan Mat INCOSXL for GC-MS studies, a PerkinElmer 2000 for the FT-IR, and a Bruker AC80 for the NMR analysis. Kinetic runs were conducted in a Chemical Data System (CDS) custom-made pyrolyzer comprising an insulated aluminium block fitted with a platinum-resistance thermometer and a thermocoupler connected to a Comark microprocessor thermometer. The temperature of the aluminium block was controlled by a digital Eurotherm 093 precision temperature regulator. It is to be noted that aluminium was chosen for its low temperature gradient and resistance to elevated temperatures. HPLC analysis of kinetic runs was carried out on a Bio-rad Model 2700 coupled with a Bio-rad 1740 UV-vis detector.

Kinetic measurements and product analysis

Procedures for kinetic measurements and data treatment and analysis of pyrolysates using flow-reactors have been described in detail elsewhere (9*a*, 10*b*, 19). Reaction products were obtained in sealed-tube pyrolyzers. Acetonitrile was used as the solvent for both kinetic and reaction product studies, and either benzene or 1,2,3-trichlorobenzene as the internal standard in the quantitative chromatography measurement of the extent of the reaction.

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